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ADVANCES IN DIAGNOSIS AND TREATMENT OF SURGICAL PULMONARY DISEASE

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Although the majority of thoracic diseases that are potentially surgical come within the scope of the thoracic surgeon, it is evident to all practitioners that lesions of the chest that are amenable to surgical therapy must be recognized early. Obviously, proper care of the patient with chest disease cannot be carried out otherwise. Since the limit of this paper does not permit discussion of the diagnosis and treatment of chest disease in detail, consideration will be given only to some of the more recent advances in management of those lesions of the lung, pleura, and tracheobronchial tree that are frequently encountered by the surgeon and are of particular interest to the medical profession as a whole.

CARCINOMA OF LUNG

Diagnostic methods for the detection of carcinoma of the lung have been perfected to such a degree that one can expect a positive diagnosis in approximately 85% of the cases. The history of cough, pain, and hemoptysis should demand that first consideration be given to carcinoma in the differential diagnosis of mass lesions of the lung. One must not wait for weight loss, lassitude, and other manifestations of inoperable carcinoma. Radiological study of the chest by the usually accepted techniques will demonstrate in most instances an atelectasis, the result of bronchial obstruction due to an endobronchial lesion, an obstructive emphysema, or the existence of a solitary mass. By means of angiocardiography, Keil and Schissel [1] have developed a technique of differentiation between unresolved pneumonia and bronchogenic carcinoma. Their procedure may prove useful also in visualizing the vascular structures of the mediastinum as well as detecting hilar lymph node enlargement due to metastasis. Vascular stenosis indicative of the encroachment of malignant tissue may also be revealed. Changes in the peripheral vascular pattern may serve to indicate the presence of a peripheral tumor or other lesion.[2]

Fifty per cent of the cases of pulmonary carcinoma can be diagnosed bronchoscopically.[3] In addition to the direct visualization of the lesion, biopsy can be done. Bronchoscopy is again of value in the visualization of the vocal cords for mobility, of the carina for infiltration, of the major bronchi for possible displacement, and of bronchi or trachea for compression by extraneous lesions.[4] These secondary changes may indicate to the bronchoscopist the presence of an extrabronchial mass or of an infiltrating one. Any carcinoma, easily diagnosed by direct observation through the bronchoscope, is probably incurable.

Cytological study of sputum and bronchial secretions may be expected to show an increase in the number of accurate preoperative diagnoses by at least 20%.[5] Carabelli reports 82.4% to 92.5% correct diagnoses in pulmonary neoplasms through cytological study of endobronchially-obtained secretions.[6] Some clinics report that an 85% incidence of positive diagnoses is obtained by use of Papanicolaou smears of bronchoscopically-obtained material and coughed-up sputum.[7] In cases of accessible lesions, needle biopsy of the lung may permit positive diagnosis. This method has been challenged because of the danger of spread or of contamination or the production of a pneumothorax. However, Rosemond and co-workers [3] report a series of 132 cases of needle biopsy without apparent complications. The operative

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1. Keil, P. G., and Schissel, D. J.: The Differential Diagnosis of Unresolved Pneumonia and Bronchogenic Carcinoma by Pulmonary Angiography, J. Thoracic Surg. **20**: 62 (July) 1950.
2. Steinberg, I.; Dotter, C. T., and Andrus, W. DeW.: Angiocardiography in Thoracic Surgery, Surg., Gynec. & Obst. **90**: 45 (Jan.) 1950.
3. Rosemond, G. P.; Burnett, W. E., and Hall, J. H.: Diagnosis of Carcinoma of the Lung, J. Internat. Coll. Surgeons **14**: 100 (July) 1950.
4. McReynolds, G. S.: Malignancy of the Lungs: I. Value of Bronchoscopy, Texas State J. Med. **46**: 872 (Dec.) 1950.
5. Ellis, F. H., Jr.; Woolner, L. B., and Schmidt, H. W.: Metastatic Pulmonary Malignancy: A Study of Factors Involved in Exfoliation of Malignant Cells, J. Thoracic Surg. **20**: 125 (July) 1950.
6. Carabelli, A. A.: Endoscopic Collection of Neoplastic Cells and Tubercle Bacilli from the Bronchi (Description of New Irrigation-Suction Collector and Anatomical, Physiological, and Pathological Factors Involved), Dis. Chest **18**: 98 (Aug.) 1950.
7. Shaw, R. R.: Early Detection of Bronchogenic Carcinoma, Dis. Chest **18**: 185 (Sept.) 1950.

mortality rates with pneumonectomy for carcinoma of the lung have now been reduced in most clinics to about 5%, which compares favorably with the operative mortality rate for carcinoma of the stomach. This low operative mortality should furnish adequate reason for emphasis now to be placed on early diagnosis, if there is to be any further improvement in survival rates following pneumonectomy for lung carcinoma.

Harrison,[8] quoting Ochsner, reports that, of every three patients who are sent to a surgeon with carcinoma of the lung, one has an obviously inoperable lesion, in one the lesion proves nonresectable, and one has a resection. This report certainly proves that patients are reporting to their family physicians too late after the onset of chest symptoms and that physicians are spending too great a period of time in the diagnosis of such lesions. Shaw [7] estimated that the average time elapsing between the appearance of symptoms and the first visit to a physician by such a patient is five months and that the average time spent in diagnosis of the disease is six months. It seems obvious, therefore, that many of these lesions become inoperable during this lengthy period. It is recommended that any mass lesion of the lung that cannot be definitely diagnosed during two or three weeks of observation should be examined by exploratory thoracotomy with direct biopsy if necessary.

Pneumonectomy has generally been accepted as the type of operation indicated in dealing with pulmonary carcinoma. However, lobectomy seems to have an advantage when uncertainty of diagnosis exists and in those instances in which pulmonary and cardiac reserve has been diminished, provided, of course, that the lesion in question can be excised by this method. This less drastic operation would seem indicated also for small peripheral lesions that have no lymph node extension and for more extensive lesions in cases in which only palliation can be achieved by excising the bulk of the tumor.[9] Effler, quoting Adams, reports that in carefully selected cases the results following a lobectomy compare favorably with those following a pneumonectomy.[10] Indeed, Churchill [9] reports a 19% five-year survival rate following lobectomy as compared with a 12% survival rate following pneumonectomy. The importance of placing emphasis on diagnostic and therapeutic measures for the management of carcinoma of the lung is evident when one realizes that this disease comprises 7% of all cases of carcinoma seen at autopsy.[11]

TUBERCULOSIS

Recently Katz and Lifschultz [12] described a method of bone marrow study for the diagnosis of acute hematogenous tuberculosis of pulmonary and extrapulmonary variety. Tubercle bacilli were found by smear and culture in 84% of a series of 78 cases. This method may prove to be valuable in the diagnosis of pulmonary tuberculosis of the hematogenous variety before obvious organ localization occurs. It is being used extensively with satisfactory results at the Brooke General Army Hospital by John G. Knauer.[13]

Surgical treatment of pulmonary tuberculosis can be divided into three categories: (*a*) collapse therapy, (*b*) drainage of cavities, either open or closed, and (*c*) pulmonary resections. Many authors [14] agree that there is a definite place for pulmonary resection in the treatment of pulmonary tuberculosis but that our present limited experience with these procedures does not warrant our abandoning recognized and proved methods of surgical collapse; however, the indications for pulmonary resection are fairly well agreed upon. They are as follows: (1) thoracoplasty failure, (2) bronchostenosis and associated bronchiectesis, (3) tuberculoma, (4) lower lobe disease, (5) upper lobe disease unsuited for thoracoplasty, and (6) questionable diagnosis.

Lobectomy and segmental resection are to be preferred to pneumonectomy except in cases in which such extensive disease exists that the problem cannot be dealt with by more limited procedures. Gebauer,[15] in several cases, has used with good results wire-enforced dermal grafts for the correction of healed tuberculous bronchostenosis. Experience with this operation is, of course, limited, and surgical extirpation seems at the present time to be the more warranted procedure. Segmental resection of involved areas and lobectomy in cases in which the main lobe bronchus is involved have both been successful in dealing with tuberculous bronchostenosis.

As indicated by its designation, segmental resection is a procedure wherein only the bronchovascular components that combine to form a lobe are removed.[14i] It is of value in those cases in which the disease is limited to one or two anatomical segments of the lobe. The advantage of segmental resection lies in the minimal sacrifice of pulmonary tissue necessary to the success of the operation. Segmental resection is equally applicable to those other indications for pulmonary surgery when the criteria of segmental limitation can be fulfilled.

The solitary circumscribed shadow of the tuberculoma is readily confused with the peripheral type of pul-

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monary carcinoma. Culver and co-workers [16] have differentiated tuberculomas into a surgical and a nonsurgical group on the basis of calcification. We feel that any peripheral lesion that is not well calcified or proved to be nonmalignant should be resected segmentally, if possible, or dealt with by lobectomy or pneumonectomy.

Tuberculous lesions of the lower lobe form a group particularly suitable for resection because the anatomic location of the lesion makes them unsuited for thoracoplasty. Certain upper lobe lesions that may prove to be more suitable for resection than for thoracoplasty include (*a*) tension cavities, (*b*) scattered nodular infiltrates with fibrosis and with indistinct areas of rarefaction, suggesting small cavities, which are usually firm and inelastic, (*c*) lesions so situated in the lobe as to require an extensive thoracoplasty with needless sacrifice of pulmonary tissue, (*d*) some giant cavities, especially those in the gutter, and (*e*) progressive caseous pneumonic disease limited to an upper lobe, occurring in children or young adults.[14b] Further experience with primary resection of upper lobe lesions is necessary, however, to permit full evaluation of this procedure.

In cases in which a lesion is suspected but not proved tuberculous and in which there is the possibility of an existing carcinoma, the patient should be subjected to exploration of the chest.

Streptomycin [17] is a proved valuable adjunct in surgery of pulmonary tuberculosis. The incidence of complications and of morbidity has been greatly reduced by its use, both preoperatively and postoperatively. As to the value of viomycin [18] in the treatment of tuberculosis clinically, a final estimate cannot be made, since a more prolonged and a more definite clinical trial must be awaited. This drug has been shown to be active against mycobacteria, both in vitro and in vivo, and its toxicity in humans is apparently not very great. The manifestations of toxicity that do occur are renal irritation, abnormalities of serum electrolytes, elevation of blood urea nitrogen, and occasional impairment of vestibular function. Preliminary studies suggest that these are reversible changes.[18f]

Segmental resection, lobectomy, and pneumonectomy have a definite place in the surgical treatment of pulmonary tuberculosis, provided one chooses his cases carefully and never forgets that he is removing only a major focus of a more widely disseminated disease.

ARTERIOVENUS FISTULA

Arteriovenous fistula of the lung is a clinical entity that has been recognized for only a few years. Apparently this pulmonary lesion represents a manifestation of a more general telangiectatic tendency. Patients with this illness usually are thought first to be suffering from congenital heart disease, because of their polycythemia, digital clubbing, and cyanosis.[19] Polycythemia vera may also be considered.[20] After the heart has been proved normal and after the x-ray has demonstrated a pulmonary lesion, the diagnosis of arteriovenous fistula of the lung should be made.

There is usually a loud murmur over the pulmonary lesion. Removal of the involved portion of the lung will result in immediate loss of cyanosis, a return of the blood cell count to normal, and a consequent cure of the patient.

CYSTS OF THE LUNG

Cysts of the lung may be either of two types, congenital or acquired. The latter type is the result of subpleural rupture of adjoining alveoli, forming blebs or bullae.[21] The two types may be differentiated pathologically by the observation of lining epithelium and elements of lung tissue within the wall of the congenital cyst. Potts and Riker [22] have described cystic-appearing areas in the lungs of infants with staphylococcic pneumonia. Cysts of either the congenital or the acquired type should be excised if symptoms are occurring because of the size of the lesion, the complication of infection or of hemorrhage, or because of a spontaneous pneumothorax. Pneumatoceles resulting from staphylococcic pneumonia apparently resolve spontaneously. Whether segmental resection, lobectomy, or pneumonectomy is indicated must be determined in each case.[23]

CHRONIC EMPYEMA

Decortication [24] has been used in the treatment of tuberculous and mixed empyemas with some success; however, it is in the case of the neglected hemothorax that decortication operations have been most successful, and in these the best functional results have been obtained. Development of the technique of pleural decortication has given us a method whereby the chronic empyema can frequently be successfully dealt with. By means of this operation, the collapsed lung of chronic spontaneous pneumothorax can be re-expanded, provided that at the time of decortication the leak in the lung is simultaneously sutured.[25] Thoracic scoliosis resultant from chronic empyema can be corrected and frequently

17. Day and others.[14b] Chamberlain and Klopstock.[14c] Munz and Adelman[14f] Hughes and others.[14h]

18. (*a*) Finlay, A. C., and others: Viomycin, a New Antibiotic Active Against Mycobacteria, Am. Rev. Tuberc. **63**: 1 (Jan.) 1951. (*b*) Bartz, Q. R., and others: Viomycin, a New Tuberculostatic Antibiotic, ibid. **63**: 4 (Jan.) 1951. (*c*) Ehrlich, J., and others: Antimicrobial Activity of Streptomyces Floridae and of Viomycin, ibid. **63**: 7 (Jan.) 1951. (*d*) Hobby, G. L.; Lenert, T. F.; Donikian, M., and Pikula, D.: Activity of Viomycin Against Mycobacterium Tuberculosis and Other Organisms in Vitro and in Vivo, ibid. **63**: 17 (Jan.) 1951. (*e*) Youmans, G. P., and Youmans, A. S.: The Effect of Viomycin in Vitro and in Vivo on Mycobacterium Tuberculosis, ibid. **63**: 25 (Jan.) 1951. (*f*) Steenken, W., and Wolinsky, E.: Viomycin in Experimental Tuberculosis, ibid. **63**: 30 (Jan.) 1951. (*g*) Karlson, A. G., and Gainer, J. H.: The Effect of Viomycin in Tuberculosis of Guinea Pigs Including in Vitro Effects Against Tubercle Bacilli Resistant to Certain Drugs, ibid. **63**: 36 (Jan.) 1951. (*h*) Werner, C. A.; Tompsett, R.; Muschenheim, C., and McDermott, W.: The Toxicity of Viomycin in Humans, ibid. **63**: 49 (Jan.) 1951.

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25. Brewer, L. A., III; Dolley, F. S., and Evans, B. H.: The Surgical Management of Chronic Spontaneous Pneumothorax; Report on Etiological and Surgical Treatment Employed in 15 Cases, J. Thoracic Surg. **19**: 167 (Feb.) 1950.

26. Kergin, F. G., and Dewar, F. D.: Pleural Decortication in the Prevention and Treatment of Thoracogenic Scoliosis, Arch. Surg. **61**: 705 (Oct.) 1950.

prevented by decortication of the involved hemithorax and application of the proper orthopedic procedures subsequently to the spine.[26]

CHRONIC SUPPURATIVE DISEASE OF LUNG

Employment of staged pulmonary resections offer patients with bilateral bronchiectasis a reasonable chance of recovery.[27] It has been found that the incidence of postsurgical complications is considerably lower in uncomplicated bronchiectasis than it is in the presence of superimposed acute suppurative disease. The incidence of bronchial fistula formation is greater with acute suppuration because of the inflammatory involvement of the hilum. This is a complication that makes for poor healing of the bronchial stump.[28] Lobectomy for one side, and later for the other, is the procedure of choice.

The improvement in prognosis of lung abscess is due to three factors: (*a*) the liberal use of blood, (*b*) the use of antibiotics, and (*c*) the change of surgical technique from drainage to excision of lung abscess.[29] Very small abscesses may be removed by segmental resection or may be shelled out of their capsules.[30] However, for abscesses over 3 cm. in diameter, it is better to employ lobectomy, because of the usual associated bronchiectasis in the lobe. The question has been raised [31] as to whether segmental resection is an adequate extirpative procedure for chronic suppurative disease of the lung, such as bronchiectasis or abscess, since suppuration is usually manifest throughout the entire lobe. Segmental resection is adequate for small lung abscesses or for those involving the lingula, since actually the lingula represents a lobe anatomically. For larger abscesses, lobectomy is to be preferred.

Experience with the surgical repair of the trachea and bronchial tree has to date been limited to experimental extirpation and reconstruction of the trachea and bronchi,[32] and to the clinical application of this work by Gebauer, who with wire-enforced dermal grafts has successfully repaired bronchi stenosed by tuberculous tracheobronchitis. He has obtained limited functional results in these cases. The long-term results of this work, however, must await the test of more time. The procedure of thoracobronchotomy [33] with approach to bronchial tumors through a transthoracic route and by opening the bronchus through its membraneous portion seems a merited one. By this technique the extent of endobronchial tumors extrabronchially can be fully determined and any indicated extirpative procedures then carried out.

Pulmonary coccidioidomycosis is now being successfully treated surgically.[34] However, as indicated in the surgical treatment of tuberculosis, one must bear in mind that coccidioidomycosis is a disseminated disease and that only a major focus of the disease is being removed. Apparently, surgical removal of a pulmonary focus of coccidioidomycosis does not cause spread of the disease. Indications for surgical removal of an involved portion of lung are as follows: (*a*) persistent cavities, (*b*) rupture of cavity with pneumothorax and empyema, (*c*) persistent hemoptysis, (*d*) coccidioma, (*e*) nonexpansile lung, and (*f*) failure of medical treatment.[34b]

The alveolar cell tumor or pulmonary alveolar adenomatosis is a comparatively recently accepted entity. The relationship of this lesion to the disease of sheep, known as jagziekte, is recognized though not fully understood. Jagziekte is apparently transmitted from affected to healthy animals. Pathologically, it resembles the human disease and is thought by some to be of viral origin, because of the apparently infectious character of the lesion. In man, the lesion appears to be of multicentric origin, manifested by respiratory symptoms of cough, dyspnea, and expectoration of moderate amounts of mucoid or foamy sputum. Diagnosis is positive only with thoracotomy and biopsy of the lung. The disease is progressive and fatal, and, even though the involved lung tissue is removed, recurrence will follow. Death usually occurs from respiratory failure before metastasis.[35] Although this disease has been recognized principally because of more frequent surgical exploration of the chest, it is apparent that surgical management is not the answer in dealing with the alveolar cell tumor.

SCALENUS ANTICUS NODE BIOPSY

Mention should be made of a scalenus anticus node biopsy, a rather minor but important surgical procedure in the diagnosis of certain pulmonary diseases. Biopsy of lymph nodes over the lower end of the scalenus anticus muscles may reveal Boeck's sarcoid or carcinoma of the lung before either of these can be diagnosed by any other means.[36]

SUMMARY

Some of the commoner surgical diseases of the lung are discussed. The present accepted methods of management of these lesions are explained.

1121 Nix Professional Bldg. (Dr. Nixon).

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Changing Causes of Death in Childhood.—The so-called degenerative conditions—cardiovascular disease and cancer—now cause more deaths among children of school age in the United States than all the infectious and parasitic diseases combined. . . . Within recent years, the long-term trend of decreased mortality from infectious diseases has resulted in a change. . . . The infectious diseases are no longer more frequent than other diseases as a cause of death among school-age children. In 1948, cardiovascular disease and cancer deaths totaled 4,514 in the 5 to 19 age group, while the infectious and parasitic diseases accounted for 3,990 deaths in the same age group.—Harold A. Kahn, Changing Causes of Death in Childhood, *Public Health Reports*, Sept. 28, 1951.

RECENT TRENDS IN TREATMENT OF PULMONARY TUBERCULOSIS

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Among all the diseases to which human flesh is subjected tuberculosis still remains the first cause of death in the world. The death rate from this scourge has been markedly decreased in the United States, but the morbidity rate remains comparatively high. It might be well to remember, too, that there are places in the western hemisphere where the death rate is not 20 to 30 per 100,000, as it is in the United States, but 500 per 100,000. With modern rapid means of transportation and the consequent increase in mingling of peoples between countries, the control of tuberculosis poses an even greater problem from the epidemiological standpoint. To meet this increasing problem, and in an effort eventually to eradicate the disease, scientists and practitioners of medicine have for the past several years redoubled their efforts to find a biologic cure for tuberculosis. Any chronic disease for which there is no specific cure naturally has a multiplicity of treatments, which are used from time to time. It is well, therefore, to pause in our progress and try to evaluate the methods used in order to plot an even better and more accurate course toward final victory over our enemy—tuberculosis. Some of these methods may change in the next few months, so that much of what is written now may have to be revised before next year—just as some of what might have been written last year may be changed now. It behooves the general practitioner to keep abreast of developments in the treatment of tuberculosis and adapt the more appropriate ones to the care of his own patients. We shall now review the methods that are generally used today for the treatment of pulmonary tuberculosis, realizing that they are not to be considered the final word in the care of patients with this dread malady.

GENERAL CONSIDERATIONS

Once the diagnosis of pulmonary tuberculosis has been confirmed, assuming a reasonable degree of intelligence on the part of the patient, the first obligation facing the attending physician is to explain carefully to him some of the fundamental characteristics of his disease and advise him on a course of treatment in the light of what is known at that time about the patient's physical, emotional, and economic condition. The physician should begin to "condition" the patient for the journey ahead of him and proceed to lead him down the road to recovery.

In the treatment of pulmonary tuberculosis rest and diet are still the basic principles on which the physician builds and plans his campaign against the disease. The plan of medical care must also take into consideration the socioeconomic factors involved for these sometimes influence the methods to be used in applying the principles of therapy. Since there are many more patients to be treated than there are hospital beds in which to treat them, many will have to be cared for in their homes, and this circumstance may lead to modifications in the treatment regimen. This condition should not, however, be a cause for withholding expert care from the home patient. With the exception of major surgical procedures, such care can be given, even though it causes the attending physician and the patient's family some inconvenience.

For those of us who have lived through several "sure cures" for tuberculosis, further new methods of therapy may be met with understandable skepticism. There are, however, measures that deserve serious attention and evaluation from time to time. At intervals since the time of Hippocrates attention has been given to diet in tuberculosis. Many special diets have been devised, with the view of giving the patient's tissues increased resistance against the tubercle bacillus and of improving his general nutrition. None have had any specific effect on the outcome of the disease. It may be mentioned in passing that while the use of extra proteins in the form of hydrolysates in preparing the patient for surgical intervention may be helpful, the routine use of such therapy has no real place in controlling the disease.[1] It is generally believed now that uncomplicated pulmonary tuberculosis requires only a well-balanced diet, including sufficient minerals and vitamins. Tonics may be employed occasionally in an attempt to stimulate appetite, but this is best accomplished by controlling the toxemia which accompanies the more acute stages of the disease.

For the patient at home in contact with his family, the control of symptoms may become a more important factor in his care.[2] For the fever and sweats uninterrupted rest and hydrotherapy are best. Proper care of the skin is important for patients who spend most of their time in bed. Many patients can be taught to control their cough, giving way to that reflex only when it is productive, thus reducing the use of cough sedatives, which often upset the stomach and cause loss of appetite and constipation. Hemoptysis from pulmonary tuberculosis in most cases stops of itself. The patient and family must be made to understand this, so the patient will not be unduly alarmed by the occurrence of this frightening and spectacular symptom. The treatment of hemoptysis is so universally understood that it need not be repeated here. We would only caution against the injudicious use of sedatives and morphine. One has only to see a patient cyanotic and gasping for breath as he drowns in his own blood to realize the danger of oversedation in these instances. The patient should be encouraged to clear the blood from his bronchi, since the threat of the spread of the disease is more serious than the danger from the loss of blood. Pain can be relieved by the application of heat to the

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chest wall or by the administration of analgesics. It is important to explain carefully to the patient some fundamental facts about the characteristics of his disease, so the symptoms will be better understood and he will cooperate better during the long period of his treatment. During the patient's initial period of bed rest, his progress should be watched carefully to help determine what further treatment may be required.

ANTIMICROBIAL THERAPY

Here enter the newer aids in the treatment of pulmonary tuberculosis. The wise practicing physician will select those definitive measures that so far have proved of most value and adapt them to use in individual cases. Unless one has adequate facilities for research, it is best to evaluate the results of professional research scientists and use those methods that seem best suited to the needs of one's individual patients. Antimicrobial agents have earned their place in present day therapy. Many such agents have been tried. Up to the present some have not given the favorable results hoped for. Among these are terramycin, aureomycin, neomycin, mycomycin, sulphetrone® (4,4′-bis[γ-phenyl-N-propylamino] diphenylsulfone-tetrasodium sulfonate),[3] colloidal copper morrhuate, glucosulfone sodium (promin®), thiazolsulfone (promizole®), and tibione (4-acetyl-amino-benzaldehyde-thiosemicarbasone).[4] Refinement of some of these agents may make them more acceptable later. The use of streptomycin-paraaminosalicylate intramuscularly once daily for 90 days has shown some promise in a small number of patients, and it seems to delay the emergence of resistant strains of organisms.[5] Further study will be required to confirm early results.

Streptomycin, dihydrostreptomycin and paraaminosalicylic acid are the chemotherapeutic agents of choice at the present time. When used judiciously they give more hope of controlling the disease and bringing an "arrest" than any other drugs we now have at our disposal. One must know their potentialities for harm as well as their power for good before risking their use.[6] The choice of a chemotherapeutic agent and the time of its use present a problem in treatment of pulmonary tuberculosis. Particularly should one consider the toxicity of the drug, the possibility of emergence of resistant strains of organisms, and concomitant therapeutic measures to be used. Given in doses of 2 to 3 gm. daily, dihydrostreptomycin is less toxic than streptomycin, and also less effective. In some series of cases a strain of germs resistant to dihydrostreptomycin developed in over 40%. In another series streptomycin given alone effected about 80% incidence of resistance at the end of 120 days of treatment.[7]

Streptomycin has been found the most effective single agent so far in treatment of tuberculosis.[8] Its therapeutic effects are largely due to the suppression of the tuberculous infection, with prevention of new lesions, but without producing a biologic cure; nor does it give assurance against relapse. Results with this drug are largely dependent on the character of the disease—it works better in the acute phases and in mucous membrane tuberculosis.[9] The drug does sometimes help in chronic tuberculosis, especially in conjunction with collapse therapy. The present trend is toward smaller doses given intermittently, that is, 1 gm. every other day or twice weekly.[10] The administration of 10 to 12 gm. of paraaminosalicylic acid (PAS) by mouth daily, with intermittent injections of streptomycin, is rapidly gaining favor with phthisiotherapists. Given in this fashion, resistance is delayed, and the patient derives benefit from the drugs over a longer period of time.[11] This treatment regimen is particularly valuable in preparing a patient for major thoracic surgical intervention and should be continued through the time of the surgical procedures and for several months afterward. In this way many patients are enabled to receive the benefits of surgical intervention who otherwise would be very poor risks indeed. Combined intermittent streptomycin therapy gives encouraging results as viewed on the roentgenogram; the "conversion" rate of sputum is highest, and the toxicity is less. In general, the efficacy of antimicrobial therapy decreases with the chronicity of the disease and to a lesser degree with the extent of the disease. It seems unnecessary to warn that evidences of toxic manifestations should be watched for all during the course of streptomycin and for a short time afterward.

We believe that it is safe to advise against the routine use of streptomycin in minimal cases of tuberculosis. Most of the patients will recover with the more conventional regimen, and it is not wise to run the risk of developing in them a streptomycin resistant germ. Some very interesting work has been reported recently in which patients were given streptomycin intermittently and paraaminosalicylic acid daily for 12 to 17 months, and then the residuals of their disease were resected in an attempt to obtain a biologic cure. While the early results are rather striking, this method of treatment needs to be studied further before proper evaluation can be made. The method presents a different concept of the "cure" of tuberculosis.

COLLAPSE MEASURES

In addition to chemotherapy, or in conjunction with it, collapse therapy occupies an ever increasing place of importance in the care of the tuberculous patient. Collapse therapy may be used to provide local rest, to correct an unfavorable mechanical situation, such as the presence of a cavity, to accelerate the healing process, or to tailor the thoracic wall to fit the functioning lung. One of the older forms of collapse therapy is artificial pneumo-

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thorax. In the last few years the indications for its use have been rapidly constricted. In some hospitals now it is almost as hard to demonstrate artificial pneumothorax to medical students as it is to find a patient with typhoid fever or smallpox for their clinical instruction. We do not believe, at the present time at least, that this form of therapy should be abandoned entirely because in selected cases we still see good results from its use. Perhaps a part of its disfavor at present is due to its former misuse, as well as the development of other methods of collapse. Pneumothorax should not be attempted until the acute febrile reaction to the disease has subsided. To do otherwise invites complications that in themselves hinder the progress of recovery and may cause the abandonment of the treatment that was counted on to bring relief.

Pneumothorax finds its chief place in predominately unilateral lesions. Subapical cavities with surrounding pneumonitis often yield to this type of therapy. A lesion that fails to regress under sanatorium care, especially if the sputum remains positive, may improve when a successful pneumothorax is established. Where there is bilateral disease pneumothorax may be employed on the better side to prepare the patient for surgical intervention on the worse side. The hoped for results with pneumothorax are selective collapse of the diseased area and partial functioning of the normal portion of the lung.[12] This collapse is then maintained over a period of years, during much of which time the patient carries on his normal pursuits. As soon as the lesion is considered firmly healed, the lung is slowly reexpanded. The evaluation of the effectiveness of a pneumothorax must be made in the first few weeks following the initial puncture. Pleural adhesions present must be cut and an effective collapse established. If this cannot be accomplished, it is a wiser course to reexpand the lung early, thus avoiding what may be dangerous complications and sparing the patient expense and loss of time in starting a more effective form of treatment. For a pneumothorax to be considered successful, cavities must close and sputum must become negative. We consider the following as reasonable indications for the early reexpansion of a pneumothorax: (1) pleural adhesions that cannot be cut safely; (2) persistent pleural effusion; (3) cavities that persist or enlarge; (4) atelectasis of underlying pulmonary tissue; (5) recurring spontaneous collapse; (6) thoracoscopic discovery of subpleural tubercles.

Any one of the above conditions spells failure for the pneumothorax and may lead to one or more of the following complications: (1) empyema; (2) spontaneous pneumothorax; (3) unexpandable lung; (4) obliterative pleuritis; (5) air embolism. It is much wiser and a more courageous procedure to tell the patient frankly that the treatment is not accomplishing what was hoped for than to persist in carrying on an unsuccessful regimen that may endanger his chances of recovery. It is believed today that 75 to 80% of the patients with pulmonary tuberculosis will not be benefited by pneumothorax. These patients are the ones with (1) pleural symphysis; (2) tuberculous pneumonia; (3) tuberculous bronchitis with evidence of bronchial obstruction[13]; (4) extensive pulmonary destruction; (5) tension cavities; (6) tuberculoma or tuberculoma-like cavities; (7) acute pleurisy with effusion; (8) dyspnea due to emphysema or decompensated cardiac disorders. These contraindications obviously severely limit the number of patients suitable for pneumothorax treatment.

PULMONARY RELAXATION

The value of diaphragmatic paralysis in the treatment of tuberculosis has been under discussion for many years. It seems fair to state that mere relaxation of the diaphragm could not be expected to yield a great influence on pulmonary lesions. Yet the addition of this therapy may be enough to allow a lesion to heal which would not heal without this aid. As a rule diaphragmatic paralysis should be temporary, since permanent loss of diaphragmatic function, with no assurance of healing the tuberculous lesion, is a gamble not worth taking. With proper understanding of the anatomy of the phrenic nerve, it can be interrupted in such a way that function should return in all but a very few cases within six to eight months. If it is advisable to continue the paralysis beyond that time, the operation can be repeated. Perhaps the most widely accepted indications today for diaphragmatic paralysis are: (1) as an adjunct to bed rest in early lesions; (2) in some patients with cavity when a more definitive collapse measure cannot be used; (3) in certain lower lobe lesions; (4) in conjunction with pneumothorax or pneumoperitoneum; (5) occasionally to help obliterate pleural space in the presence of empyema. There is some disagreement among the profession even on these indications.

The observation that air introduced into the peritoneal cavity accidentally had a beneficial effect on tuberculous lesions in the lungs has led to the use of artificial pneumoperitoneum as a primary procedure or as an adjunct to phrenic nerve surgery. In the last three to four years there has been in many places throughout the country a noticeable shift in treatment from pneumothorax to pneumoperitoneum. The indications for both are changing from month to month, but in all probability there will be a leveling off period soon. At the present time this procedure is indicated: (1) in minimal lesions, especially acute exudative ones, as an adjunct to bed rest; (2) in moderately advanced lesions with small or moderate-sized cavities when pneumothorax has failed; (3) in advanced bilateral cases too extensive for other collapse therapy; (4) to control exudative lesions prior to thoracoplasty; (5) in the old age group with complicating emphysema; (6) to help obliterate empyema cavity; (7) in basal lesions beneath upper thoracoplasty; (8) after resection.

This form of therapy is contraindicated in cases of heart failure, in moribund patients, during the latter months of pregnancy, in the presence of large abdominal tumors, or in the presence of uncontrolled hernias. The relaxation and elevation of the diaphragm afforded by the procedure may favorably influence the course of the disease so that a more definitive measure can be used later. Its use should be discontinued if significant ascites occurs, or if the patient finds it seriously interferes with eating. Serious complications with this therapy are rare, and it can be discontinued easily.

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SURGICAL TREATMENT

Surgical intervention in the treatment of pulmonary tuberculosis occupies a unique position in the field of surgery, in that it is not in itself definitive, but is merely an adjunct in the treatment of patients with this disease. Major surgical procedures used in the treatment of tuberculosis are of two general types: (1) those operations whose effect on the lung are direct, such as collapse therapy procedure, and (2) those operations performed on the lung itself, such as cavity drainage and resection. Formerly the patients referred to the thoracic surgeon for treatment were examples of failure of all other forms of therapy. This failure was due to late diagnosis, too little attention to the minimal lesion, and inadequate bed rest. There has been a tendency in the past to plan therapy according to a routine in which major surgical measures have been used only when other methods have been tried and failed. This concept does away with case selection and implies that the simpler procedures are harmless and in no way interfere with the success of major procedures. The old trial and error method is no longer justifiable.

The aim of all treatment of tuberculosis is the complete and permanent control of the disease and the return of the patient to a state of health consistent with comfort and a reasonable level of activity. Although surgical intervention is considered only an adjunct to treatment, it plays an increasingly important role in the management of patients with tuberculosis. Now tuberculous patients are considered for some type of collapse or surgical intervention, with the exception of those whose disease is so minimal that such treatment is not necessary or those whose disease is so far advanced that therapy of this type is impossible. Surgical intervention in tuberculosis is designed to augment the healing process through relaxation of diseased tissue by collapse, drainage, or actual resection of the major focus of the disease. Relaxation may be all that is necessary to bring about complete healing, but chronic cavernous areas may need collapse. Cavity closure and resultant sputum conversion are the chief criteria of success in the treatment of pulmonary tuberculosis. One does not, however, overlook such important factors as the general nutrition of the patient and the eradication of all signs of activity of the disease.

Cavity closure may be influenced by many mechanical factors. Tuberculous tracheobronchitis is perhaps the most important factor operating within the lung which influences the closure of cavities. Obstruction of the bronchial lumen by ulcerating tissue and bronchial secretion may cause a valve-like action which places cavity areas under positive pressure. Such cavities resist closure, and unless this mechanical factor can be removed, it may be difficult to obtain a good result. The cavity wall may be so thick that closure will be impossible by collapse. In these tuberculoma-like cavities nothing but excision will suffice. The extent of the pericavernous involvement may influence the time taken to bring about cavity closure, so that one would have to wait a longer period for sputum conversion here than in patients having cavities with thinner walls and less extensive involvement of adjacent tissue. The anatomic extent of the pulmonary lesion influences decisions regarding surgical intervention. The disease may be so minimal that surgical intervention would not have to be contemplated, or the extent of the disease may be so great as to render surgical intervention inadvisable, since there would be insufficient functioning pulmonary tissue to support life after the surgical program had been completed. Between these two extremes, however, there exists a group of patients who have disease of various extent who are suitable for surgical procedures that have been devised for the treatment of pulmonary tuberculosis. The general advance of the disease or deterioration in the condition of the patient may contraindicate or be cause for abandoning collapse therapy. The type of lesion, too, becomes an important factor in selection of cases for surgical intervention. The physiological as well as the chronological age of tuberculous patients must be considered. Thoracoplasty is a badly deforming operation on patients in the growth period and should not be used with these patients. Advanced age may not absolutely contraindicate certain of the major surgical procedures, but it might make them inadvisable in individual cases. The patient's immunologic response to the disease must be estimated. Pulmonary tuberculosis is a disease characterized by exacerbation and remission. The timing of the application of the various surgical procedures must be considered carefully in order to perform the operation at the time when the patient is in the best possible condition. Rest and chemotherapy are of great value in this regard. The patient's economic situation must also be considered. Some types of treatment must be continued over a period of months or years and entail considerable expense. Often the choice between two procedures, both of which offer a good chance of success, may be made purely on the economic basis. The temperament of the patient and his ability to cooperate may influence decision as to therapy. There are some people who are not temperamentally suited for an extensive period of treatment, which requires a great deal of self-discipline. In patients of this temperament a permanent type of collapse may be preferable.

Thoracoplasty has proved to be one of the most successful procedures in the surgical treatment of patients having pulmonary tuberculosis.[14] The technique of this operation has been greatly refined so that the mortality is now less than 3%, and the good results that can be expected are in the neighborhood of 80 to 90%. This lowering of the mortality and increase in good results has been accomplished in spite of the fact that much poorer risk patients are now accepted for this procedure. Performing the operation in small stages instead of one large heroic surgical procedure has undoubtedly been the greatest contribution to the safety of this operation. A thoracoplasty should obtain adequate collapse and yet conserve as much pulmonary function as possible. Before a patient is accepted for thoracoplasty, he must be carefully evaluated from the standpoint of respiratory reserve to make sure he can tolerate the full program contemplated. It is an injustice to the patient to start a procedure if it stands very little chance of being completed.

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Thoracoplasty is indicated in patients having cavernous disease in one lung in whom the other lung is free of disease, or the disease is at least quiescent. Thoracoplasty also may be useful to bring the disease gradually under control. It may be done with the realization that it probably will not bring about conversion of sputum. It may be undertaken with the frank realization that resection may be necessary as a later procedure. Thoracoplasty may be indicated to alter the chest wall in order to permit maximum use of the residual functioning pulmonary tissue in patients who have destroyed lungs or who have had resections. Absolute contraindications to thoracoplasty that are most generally accepted at present are: (1) extensive active disease in the contralateral lung; (2) inadequate respiratory reserve; (3) associated nonpulmonary disease of grave prognosis; (4) large solitary basal cavities; (5) tuberculoma and tuberculoma-like cavities; (6) tuberculous granulomas in the trachea and contralateral bronchi. Relative contraindications to thoracoplasty are: (1) minimal disease; (2) stenosis of a major bronchus; (3) bronchiectasis producing symptoms; (4) patient in growth period of life; (5) severe exudative tuberculosis; (6) advanced age; (7) cyst-like cavities which are probably epithelialized. This last group of contraindications are classified as "relative" because conditions conceivably can change so that they may no longer prove contraindications. While the results of thoracoplasty are improving from year to year, it must not be assumed that this operation is free from trouble. The following complications may occur: (1) spread of the disease; (2) atelectasis; (3) hemothorax due to tearing of the pleura; (4) wound infection; (5) inordinate postoperative pain; (6) loss of shoulder motion; (7) scoliosis; (8) dyspnea due to loss of respiratory reserve.

The extirpation of tuberculous lung tissue is not a new idea, but most of the knowledge and experience with this method of treatment have been gained in the last 10 years, during which time it has been used with increasing frequency. During the earlier part of this period, results were discouraging because of the relatively high operative mortality or the prohibitive incidence of serious complications. More recently, however, significant advances have been made in thoracic surgery and the fields of anesthesiology and bronchoscopy, so that the mortality and complications associated with lung resection have been markedly reduced. In fact, pulmonary resection can be performed today with such safety that it should be considered in any therapeutic program for the tuberculous patient. It should be stated that pulmonary resection is not a competing but a supplementary form of treatment to the established methods of rest and collapse therapy. In general, it can be used when simpler measures fail or cannot be expected to control the pulmonary lesion. It is difficult just now to present a categorical list of indications and contraindications for resection, but the most generally accepted indications today are: (1) bronchial stenosis sufficient to block drainage of the lung; (2) bronchiectasis complicating tuberculosis; (3) cavities in the lower lobes with the other lobes relatively clear; (4) tuberculomas or tuberculoma-like cavities; (5) epithelialized cavities; (6) post-thoracoplasty resection.

Where it can be employed, resection has some advantages over thoracoplasty—such as rapid conversion of sputum, fewer operative procedures, less deformity, and effectiveness where thoracoplasty would likely fail. It should be repeated though that resection does have the disadvantage at present of a higher mortality and a higher complication rate. One of the disadvantages of resection is that it forces other portions of the remaining lobes to overdistend to accommodate the remaining space. Many surgeons now attempt to overcome this disadvantage by performing a thoracoplasty on every patient who has had a lobectomy or pneumonectomy. It may be that this combination can supplant thoracoplasty as a procedure of choice in handling many patients with far-advanced tuberculosis. The two major complications of resection, pleural infection and spread or reactivation of disease, have been eliminated largely by careful technique, improved anesthesia, and the adjunct of antimicrobial therapy. It seems preferable at the present state of development to do a thoracoplasty instead of a resection in any patient in whom thoracoplasty conceivably can bring about good final results. This contention is supported by the experience that thoracoplasty patients in general do well and that the longer a series of thoracoplasties is followed the more good results will be found. In contradistinction to this, resection for tuberculosis seems to follow a line of diminishing returns, in that the longer any series of resections is followed the fewer good results are found.

Early surgical attempts to drain tuberculous cavities led to disastrous results. It was found that the opening of these cavities led to the introduction of secondary infection, so that the patient became much sicker and also had a painful draining wound. In an attempt to overcome the mechanical problem provided by blocked or tension cavities, Monaldi recommends drainage of such a cavity through the chest wall. Through a cannula a catheter is introduced directly into the cavity through the chest wall and is held in place after the cannula is withdrawn. Such drainage may reduce cough and toxemia and also improve the patient's general condition. Since the discontinuation of the suction often allows the cavity to reopen, the use of Monaldi drainage supplemented by thoracoplasty collapse is favored by many surgeons as a means of closing large tuberculous cavities. Cavity drainage by rib resection is a useful procedure in a very few patients who have had unsuccessful thoracoplasties or in whom thoracoplasty is contraindicated because of poor respiratory reserve or because of the position of a tuberculous cavity. As a rule these cavities must be drained by the use of a two stage technique to make sure there is proper pleural symphysis before the cavity is opened. Cavities are packed and treated in the same manner as a pulmonary abscess. The use of streptomycin mixed with plasma as a dusting powder will reduce the infection around the drainage site. This procedure is advocated as a means of salvaging a very small percentage of patients who cannot get well in any other way.

The necessity of performing thoracoplasty in several stages and the resulting deformity caused by thoracoplasty has led to a continuing search for an operation which will yield as good results without these disadvan-

tages. Various operations creating collapse by separating the parietal pleura from the endothoracic fascia have been devised. The maintenance of the space has been accomplished by the use of a variety of materials—i. e., air, oil, paraffin, fat, muscle, and plastic balls. Regardless of the space filling material used, all these operations have certain disadvantages compared with thoracoplasty. They are not safe over large cavities where the lateral wall of the cavity may be receiving some of its blood supply from the intercostal vessels. In these patients rupture of the cavity into the extrapleural space is not uncommon and results in a severe complication. Frequently a thick-walled cavity may be displaced downward by the extrapleural operation without closing it, which leaves an almost impossible therapeutic problem. Extrapleural operations have a limited number of indications in which maximum preservation of vital capacity is necessary in order to use another procedure to control disease in the opposite lung. While this treatment may be very useful to aid in arresting disease in a small group of patients with bilateral lesions, as a procedure by itself it certainly should not supplant thoracoplasty.

SUMMARY

In this paper attention is called to the fact that tuberculosis still presents a major health problem in the world today. There are certain basic fundamentals of treatment to be observed, the chief of which is rest. Great improvements in phthisiotherapy have been made in recent years through chemotherapy and collapse treatment. Surgical measures have brought to the field of tuberculosis therapy great aid and much encouragement in our struggle to eradicate this disease. Some of the indications and contraindications for measures in the present day treatment of tuberculosis are given, with the full realization that they may change from year to year as progress is made through further experience. The practicing physician is urged to study these measures, so that he may at all times adapt them to the best care of his patients.

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RECENT DRUG THERAPY IN DISEASES OF THE CHEST, INCLUDING TUBERCULOSIS

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At present, there are a number of effective drugs available for the treatment of many of the common acute pulmonary infections; for example, Pneumococcus pneumonia can be controlled successfully by sulfadiazine, penicillin, aureomycin, chloramphenicol, or terramycin. It is desirable in many cases of pneumonia and in other types of pulmonary infection to determine the exact etiological agent and its sensitivity to the various antibiotics before beginning treatment. Unfortunately, this is frequently impossible because the patient's condition requires immediate therapy or laboratory facilities to perform the tests are lacking. Most hospitalized patients suffering from pneumonia now receive penicillin because of its low toxicity and low cost; however, in most cases, the advantage of oral administration is so great that any one of the three latter antibiotics are likely to become even more popular than they now are, if their cost is reduced. Since aureomycin, chloramphenicol, and terramycin have a broad antibacterial spectrum, there is an additional advantage in their use, if the exact etiological diagnosis is uncertain. Penicillin is likely to be strikingly beneficial only in pneumonias caused by pneumococci and streptococci. Although staphylococcic pneumonias are sometimes amenable to this treatment, they are often caused by penicillin resistant organisms. On the other hand, aureomycin, chloramphenicol, or terramycin control not only pneumococcic, staphylococcic, and streptococcic infections but also influenzal, coliform, tularemic, and Friedlander's pneumonias. Pneumonias associated with Q fever, typhus fever, and spotted fever are also favorably influenced, as are primary atypical pneumonia and pneumonia associated with psittacosis and lymphogranuloma venereum.[1] Although the evaluation of antibiotic treatment of primary atypical pneumonia has been difficult because of its variable clinical course and generally good prognosis, controlled studies indicate that aureomycin is valuable in shortening the period of illness.[2]

Streptomycin should not be forgotten in the treatment of pneumonias. Its value in treating tularemic infections has been known for a number of years. It is effective in Friedlander's pneumonia [3] and combined with sulfadiazine in treating influenzial infections.[4] In an uncontrolled series of cases, it was reported effective in the treatment of primary atypical pneumonia.[5] It has also proved to be the most valuable antibiotic in the treatment of plague.[6]

Lung abscess, acute, subacute, or chronic, is favorably influenced to some degree by antibiotic therapy. If properly handled, surgical intervention is unnecessary in most acute and many subacute abscesses. We found that a combination of parenteral and aerosol therapy was more effective than either used alone. As a rule, two in-

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jections of 300,000 units of procaine penicillin and four aerosol treatments were given daily. The aerosol solution was made up of 2 cc. of isotonic sodium chloride solution, 3 cc. of a chlorophyll derivative (chloresium®), and 500,000 units of crystalline penicillin. One cubic centimeter of the mixture was given at each treatment. Compressed air was used to avoid the danger of possible explosion, with air flowing at a rate of 4 to 6 liters per minute, and a racemic epinephrine solution (vaponefrin®) or a DeVilbiss no. 40 nebulizer. Chloresium® was principally useful in eliminating the bad odor of sputum, but perhaps had some antibacterial action as well. Therapy was continued until complete clearing of the pulmonary lesion, as seen in the roentgenogram, had taken place or until there was no further change in the residual shadows. The period of treatment was usually four to six weeks and sometimes longer. If the residual shadows were extensive and consisted of more than a few fibrous strands, resection of the involved portion of the lung was performed, not only for the purpose of removing infected and damaged residual pulmonary tissue but also because of the danger that a pulmonary neoplasm might be the basic cause of the lesion that resembled an abscess.

In most cases, acute exacerbations of the symptoms of bronchiectasis were relieved by short periods of treatment with combined parenteral and aerosol penicillin. Oral use of aureomycin, chloramphenicol, and terramycin also proved useful. However, at present, if feasible, excision of the involved portion of lung offers the best prospect of permanent cure. Antibiotics did not influence the condition of patients suffering from nonspecific pulmonary fibrosis, except with regard to the control of superimposed bacterial infections. In the management of the chronic suppurative bronchitis and bronchiectasis associated with cystic fibrosis of the pancreas, penicillin given parenterally and by aerosol, and particularly aureomycin, were found useful.[7]

Among the pulmonary diseases due to fungi, actinomycosis was treated successfully with large doses of penicillin, and with penicillin and sulfadiazine, the latter being more effective.[8] A patient with severe, nonpulmonary actinomycosis recovered after aureomycin therapy.[9] Among the three other relatively common fungus infections in the United States that involve the lung, there is no successful treatment for disseminated histoplasmosis and disseminated coccidiosis. In treating blastomycosis, iodide therapy, with prior desensitization to the fungus in patients having a positive intradermal test result, is the only available method of treatment with any promise of success at present.[10]

To date, no drugs have been found that have a proved, permanent influence on sarcoidosis or berylliosis, silicosis, or other pneumoconioses.

Much work has been and is being done in laboratories throughout the United States in an attempt to find additional and improved drugs for use in the treatment of tuberculosis. At present, streptomycin, dihydrostreptomycin, paraaminosalicylic acid (PAS), and amithiozone (TB-1) are used widely clinically, and neomycin, viomycin, and terramycin are being studied in widespread clinical investigations. Of the drugs just mentioned, streptomycin and dihydrostreptomycin have proved the most effective. In the small doses now being given (1 gm. a day or less) one drug has little advantage over the other. They are equally effective therapeutically, and although the chief manifestations of toxicity of both involve the eighth nerve, streptomycin is more inclined to affect the vestibular branch and dihydrostreptomycin the auditory branch. The tendency of dihydrostreptomycin to cause deafness, particularly if given in large doses, was well substantiated in the case of the chloride salt of dihydrostreptomycin. That this is true of the sulfate salt of dihydrostreptomycin, which is now supplied by the drug companies, seems less likely but is still uncertain.

Paraaminosalicylic acid, when used alone in the treatment of tuberculosis, was found to be less effective therapeutically than streptomycin, but, nonetheless, of definite value. It is given orally, the usual dose being 12 gm. per day, in three or four divided doses. Toxic effects were limited to the gastrointestinal tract and consisted of dyspepsia, nausea, vomiting, and diarrhea. These were often absent and seldom severe, but, occasionally, patients were unable to tolerate the drug. Paraaminosalicylic acid is most effective when given in combination with streptomycin, emergence of tubercle bacilli resistant to streptomycin being thus greatly delayed.

Amithiozone was used extensively in Germany before being introduced into the United States. The recommended dose is 100 to 200 mg. daily, orally. Experience with amithiozone in the United States proved disappointing therapeutically. Toxic effects were common, particularly with doses of 200 mg. per day or more. There was, at times, nausea and vomiting, evidence of liver or kidney damage, anemia, and leukopenia. Any or all of these effects could occur in the same patient. When administration of the drug was stopped promptly, the toxic effects were found to be reversible in most patients. At present, amithiozone is usually reserved for the treatment of tuberculous patients who are in need of drug therapy and cannot tolerate streptomycin or paraaminosalicylic acid. Whether amithiozone, when given in combination with streptomycin, acts similarly to paraaminosalicylic acid in delaying the emergence of streptomycin resistant tubercle bacilli is still under investigation.

Neomycin, although active against the tubercle bacillus, in vitro and in vivo, has thus far proved too toxic for general use in the treatment of human tuberculosis. A high incidence of deafness and renal disturbance has occurred in the few patients treated.[11] Viomycin is highly active against the tubercle bacillus in the test tube and in the experimental animal.[12] The available data, which

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9. Wright, L. T., and Lowen, H. J.: Aureomycin Hydrochloride in Actinomycosis, J. A. M. A. **144**: 21 (Sept. 2) 1950.

10. Smith, D. T.: Immunologic Types of Blastomycosis: Report on 40 Cases, Ann. Int. Med. **31**: 463 (Sept.) 1949.

11. Carr, D. T., and others: Neomycin in Clinical Tuberculosis, Am. Rev. Tuberc. **63**: 427 (April) 1951.

12. Hobby, G. L.; Lenert, T. F.; Donikian, M., and Pikula, D.: Activity of Viomycin Against Mycobacterium Tuberculosis and Other Microorganisms in Vitro and in Vivo, Am. Rev. Tuberc. **63**: 17 (Jan.) 1951. Steenken, W., Jr., and Wolinsky, E.: Viomycin in Experimental Tuberculosis, ibid. **63**: 30 (Jan.) 1951.

are admittedly small, indicate that it is somewhat effective in human beings. However, with regard to toxic effect, in addition to the effect on the vestibular and auditory nerves and kidneys, which is similar to that of streptomycin and dihydrostreptomycin, there were marked changes in serum electrolytes, consisting of hypokaliemia, hypocalcemia, hypophosphatemia, and hypochloremia as well as an increase in carbon dioxide combining power.[13] The mechanism of the effect on electrolytes is not understood. Although its peculiar toxic effect makes the management of cases difficult and a great strain is placed on the laboratory because of the multiplicity of tests needed for safety in long-term therapy, viomycin must be studied further to ascertain its place in the chemotherapy of tuberculosis.

The effect of terramycin on human pulmonary tuberculosis was disappointing; however, there is a possibility that it may have an effect similar to that of paraaminosalicylic acid in delaying the emergence of streptomycin resistant organisms. A study of this is under way.

At present, for patients whose tubercle bacilli are still sensitive to streptomycin, combined therapy with streptomycin and paraaminosalicylic acid is preferred. If streptomycin is given in doses of 1 gm. or 0.5 gm. daily or 1 gm. twice a week, with 12 gm. of paraaminosalicylic acid daily, almost identical therapeutic results are obtained. Perhaps the regimen employing 1 gm. of streptomycin twice a week, with 12 gm. of paraaminosalicylic acid daily, is best for most patients, since toxic effects are rare, and our present impression is that streptomycin resistant organisms are at least no more likely to develop than if streptomycin is given daily with paraaminosalicylic acid.

Although there have been occasional exceptions, most patients whose tubercle bacilli have become resistant to streptomycin have not shown such good results with further chemotherapy as those whose organisms remained sensitive. After combined treatment with streptomycin and paraaminosalicylic acid for four months there were streptomycin resistant organisms in only 15% of the patients whose sputum remained positive, whereas, if streptomycin was used alone, the sputum of about 80% of such patients contained resistant organisms. In many cases, this permitted longer periods of treatment with lasting beneficial results than was possible when streptomycin was used alone.

In addition to the ototoxic effect already mentioned in connection with both streptomycin and dihydrostreptomycin, evidence of renal toxicity, as shown by the presence of albumin, casts, and red and white blood cells in the urine, occurred in a small proportion of patients. This has become less frequent because of the lower doses used at present. In most patients, the presence of urinary abnormalities was of no consequence; however, in patients with renal failure, as evidenced by the presence of a high blood urea nitrogen and impaired renal function tests, streptomycin or dihydrostreptomycin should be used with great caution, if at all, since, in such cases, there was a strong tendency for the renal function to become worse.

Chemotherapy was found to be particularly useful in the treatment of patients suffering from acute advanced pulmonary tuberculosis. Its use, for example, in massive tuberculous pneumonia completely altered the prognosis of this serious condition.[14] In fact, it is now difficult to arrive at a prognosis before chemotherapy is tried, since many patients whose death seemed certain were saved, some temporarily, others living on with the disease in a chronic form, and a few even returning to good health. Most patients with very advanced disease should undergo prolonged treatment of at least eight months to a year. Chemotherapy was particularly beneficial in tuberculous tracheobronchitis. These lesions responded rapidly, and, usually, two to four months of treatment were sufficient. Contrary to earlier experience with streptomycin alone, we found that the so-called tension cavities responded well to a combination of streptomycin and paraaminosalicylic acid, particularly if treatment was prolonged for at least eight months. Unfortunately, chemotherapy was found to have much less value in the treatment of long-standing chronic pulmonary tuberculosis, and little more than the temporary relief of symptoms may be expected in such cases.

As an approximate summary of the study of the many regimens used by the Veterans Administration and army and navy hospitals, patients suffering from advanced, relatively acute pulmonary tuberculosis, after four months of treatment with streptomycin and paraaminosalicylic acid, may expect to find roentgenographic evidence of moderate to marked improvement in about 50% of the cases, slight improvement or no change in about 40%, and evidence of unfavorable progression in about 10%.[15] After eight months of treatment, about 70% of the patients may be expected to show moderate or marked improvement.

In general, patients with minimal pulmonary tuberculosis should not undergo chemotherapy, because most of them derive as much benefit from ordinary methods of treatment. In any event, the importance of correlating chemotherapy with other methods of treatment cannot be stressed too greatly. Chemotherapy is not a substitute for prolonged bed rest, and the proper timing of the addition of collapse therapy, when appropriate, should be planned in each case on an individual basis, at the outset.

13. Werner, C. A.; Thompsett, R.; Muschenheim, C., and McDermott, W.: Toxicity of Viomycin in Humans, Am. Rev. Tuberc. 63:49 (Jan.) 1951.

14. Schwartz, W. S., and Moyer, R. E.: Management of Massive Tuberculous Pneumonia: Therapeutic Review of 75 Cases, Am. Rev. Tuberc., to be published.

15. 9th Streptomycin Conference (on the Chemotherapy of Tuberculosis), April 18-21, 1950, St. Louis, Mo., Veteran's Administration.

Myocardial Infarction.—The growing tendency to standardize the treatment of patients with myocardial infarction is probably due to fear of the infrequent but unpredictable and serious complications which occur in this condition. Such standardization seems illogical, since it is increasingly apparent that myocardial infarction is a "quantitative" disease, that is, a disease in which the extent of injury, and thus the degree of severity, the frequency of complications, and the rate of fatality differ greatly. The reported rate of fatality, for instance, has varied from 8 to 83%, the discrepancy being due, no doubt, to differences in the selection of cases and in acuity of diagnosis. Recently, the use of multiple unipolar chest and limb lead electrocardiograms has made it possible to detect myocardial infarction in patients in whom the symptoms and other signs otherwise would have been inadequate for diagnosis.—John J. Sampson, M.D., The Treatment of Myocardial Infarction, *American Practitioner*, December, 1951.

THERAPEUTIC EXPERIMENTS IN FEMALE INFERTILITY

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The therapeutic value of uterotubal insufflation has been accepted by many writers because pregnancy has many times followed soon after the procedure.

Admittedly, the possibility of a psychological influence cannot be dismissed, and true assessment of the method is difficult. Other procedures involving instrumentation of the cervical canal, such as dilatation of the cervix and hysterosalpingography, have been known for many years to be frequently followed by pregnancy.

The modus operandi of "cure" by insufflation has been discussed at length by Rubin,[1] who considers it to be due to one or more of the following effects: establishing patency of the genital tract, removal of the cervical mucous plug, dilatation of the tubes, and possible psychic effect.

Until five years ago, I performed tubal insufflation routinely, both as a diagnostic and as a therapeutic procedure in all cases of primary sterility at the sterility clinic and in the wards of the Royal Samaritan Hospital for Women. Since then, the procedure has been discontinued at the sterility clinic as a routine measure, so that comparative experiments might be carried out, not only to assess the results of other methods of treatment but also to attempt a critical evaluation of the therapeutic merits of insufflation.

My insufflation cases were derived in approximately equal numbers from the clinic and from the wards. The clinic patients received no anesthesia; the others were anesthetized. A follow-up study of routine insufflation showed that, of 893 patients traced, 262 (29.3%) became pregnant. The main features of the pregnancies may be summarized as follows. A total of 158 patients were under 30 years of age, and 104 were 30 years or older when first seen. The oldest was 42 years of age and had been married for four years; she miscarried at two months. One hundred thirty-six had been married 3 years or more, 47 had been married 5 years or more, and 1, 13 years (aged 35). No patient married for a longer period than this became pregnant. Patency had been diagnosed in 231 and nonpatency in 31 cases, with 24 of the latter patients under anesthesia and the other 7 without it. All the cases of nonpatency were seen early in the series, and these patients had received insufflation once only. The fallacy of a single finding of nonpatency is apparent from these figures. Pregnancy terminated in miscarriage in 48 (18.3%) of the patients, although 7 subsequently had a full-term pregnancy; in 1 other patient, pregnancy was terminated for hyperemesis gravidarum and in another 2 for toxemia (1 at four months and the other at seven months); 1 patient had a tubal pregnancy four years after insufflation. Thus, 217 (83%) bore a child, including 2 women who bore twins. One patient had three miscarriages, and five patients had two; none of the six has since become pregnant. In 3 of the 262 patients receiving insufflation, the date of occurrence of pregnancy could not be accurately ascertained. The time elapsing between insufflation and conception in the remaining 259 cases was as follows: 23 pregnancies occurred without an intervening menstrual period, 12 after one period, 10 after two periods, 24 after three periods, 7 after four periods, 17 after five periods, and 15 after six periods. Thus, 69 (27%) of 259 pregnancies occurred within three months and 108 (42%) within six months. During the following six months, 47 patients became pregnant. The remaining 104 pregnancies occurred at intervals varying from one to five years. Rubin [2] reported a series of 573 cases of primary and secondary sterility in which pregnancy occurred after insufflation. Within three months of the test, 265 (46.2%) became gravid and, within six months, 378 (64%) became pregnant.

In the first comparative series, a consecutive unselected series of 300 infertile women, the only treatment was the passing of an uterine sound. It was thought that this might throw some light on the "cervical instrumentation factor." Of the 253 patients treated and followed to date, 45 (17.7%) became pregnant within 12 months after the sound was passed; five of them missed their periods at once. In such cases, it is possible that conception preceded treatment. The pregnancies proceeded normally to term. In the other 40 pregnancies, 7 patients had only one period after the passing of the sound; 4 had two periods; 3 had three periods; 10 had four periods; 2 had five periods, and 4 had six periods. The remaining 10 had between 7 and 11 periods. An additional 11 patients became pregnant more than a year after the passage of the sound, 6 of them without any further form of treatment and 5 after tubal insufflation.

I followed this study with one of a similar, consecutive series of 300 patients with primary sterility in whom nothing more was done than a bimanual pelvic examination at the first visit to the sterility clinic. To date, 286 patients have been traced, of whom 31 became pregnant (10.8%); nine of them missed their periods at once. In the other 22 pregnancies, 6 patients had only one period after examination, 3 had two periods, 6 had three periods, 3 had four periods, and 2 had six periods. The remaining 2 had 9 and 11 periods respectively. In addition, two patients became pregnant more than a year after examination but after the subsequent passing of a sound.

The next series planned was a similar, consecutive series of 300 patients with primary sterility who were given intramuscular injections of "disecron" (injection containing 2.5 mg. of estradiol monobenzoate and 12.5

From the Royal Samaritan Hospital for Women.

Read before the Section on Obstetrics and Gynecology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. Rubin, I. C.: Uterotubal Insufflation: A Clinical Diagnostic Method of Determining the Tubal Factor in Sterility Including Therapeutic Aspects and Comparative Notes on Hysterosalpingography, St. Louis, C. V. Mosby Company, 1947.

2. Rubin, I. C.: Therapeutic Aspects of Uterotubal Insufflation in Sterility, Am. J. Obst. & Gynec. 50: 621, 1945.

mg. of progesterone in 1 cc. ethyloleate) over a period of six months. The injections were given every third day, commencing with the fifteenth day of the menstrual cycle as the presumptive date of ovulation until the onset of menstruation, or if the latter did not supervene, for two more weeks until a Friedman test could be performed. The preparation, made by the British branch of the Schering Corporation, is a sterile oily solution, containing 12.5 mg. of progesterone, with 2.5 mg. of estradiol benzoate (estradiol monobenzoate). The formula has been "modelled upon a method of treatment originated by Zondek." The theoretical basis for its use is that an important cause of female infertility is the failure of nidation of the fertilized ovum because of incomplete preparation of the endometrium. It is also suggested that, even though nidation occurs in some cases, the level of circulating hormones produced by the corpus luteum is inadequate to maintain pregnancy, with the result that abortion occurs at so early a stage that it may be considered as a form of sterility. The "disecron" series is as yet incomplete, 243 patients having been treated to date. In 203 patients, sufficient time has passed to endeavor to assess results; however, owing to the many attendances required and, in several cases, owing to aversion to per-

Pregnancy Percentage Rates in Groups of Sterility Cases

No. of Periods After Treatment	Insufflation Group (893 Patients)	Uterine Sound Group (253 Patients)	Bimanual Examination Group (286 Patients)	Hormone Therapy Group (143 Patients)
0.....	2.6	2.0	3.1	1.4
0- 3.....	7.7	7.5	8.4	6.9
0- 6.....	12.1	13.8	10.4	18.2
0-12.....	17.4	17.8	10.8	19.6

cutaneous injections, the default rate was high. Of 143 patients successfully or adequately treated and traced, 28 became pregnant (19.6%) within 12 months after the commencement of "disecron" injections. Two of them missed their periods at once. In the 26 other pregnancies, 3 patients had only one period after commencing "disecron" treatment; 3 had two periods; 2 had three periods; 4 had four periods; 7 had five periods; and 5 had six periods; the remaining 2 had nine periods each.

The husbands of the patients in all the groups were referred for seminal examination at the first interview with the patient; this examination was carried out in 47% of the 1,575 cases. In the husbands of the patients who had insufflation, seminal examinations showed major impairment in 25.1% and total azoospermia in 12.4%. The corresponding figures were 20.7% and 6% in the "uterine sound" group, 26.8% and 6% in the "nothing done" group, and 26.7% and 9.4% in the "disecron" group. The experimental groups also appeared to warrant comparison with each other and with the insufflation series, on the grounds of being unselected and of being statistically similar in respect to age distribution and duration of marriage.

RESULTS

In analyzing the results, I will not go beyond one year, which was the limit of the follow-up period in one of the groups. For the purpose of analysis, the "disecron" group will be reckoned as treated from the start of the series of injections. The most important comment is that three of the groups were small. Pregnancy supervened within 12 months in 17.4% of the insufflation group, 17.8% of the "sound" group, 10.8% of the "nothing done" group, and 19.6% of the "disecron" group. These figures show a decisive advantage in the three actively treated groups for the year of the follow-up (see the table).

When these figures are further analyzed, one finds that, in the first three months, the pregnancy rates were fairly uniform, ranging from 6.9% in the "disecron" group to 8.4% in the "nothing done" group. (The "nothing done" group may have shown better results owing to the fact that nine women conceived after treatment without any supervening menstruation). The advantages of the active measures were not apparent until the fourth month but then continued until the end of the year. Most notably, the "disecron" group had a pregnancy rate of 11.3% from the fourth to the sixth month inclusive, after the commencement of treatment. On the other hand, only two pregnancies occurred in the "disecron" group after completion of the six month "course."

The investigations permit us to compare two moderately large groups, the 893 patients treated by insufflation and the 682 others. The pregnancy rates in these two groups were virtually identical in the first three months, and they differed little even at the end of the year, being 17.4% and 15.3% respectively. Although in this respect the insufflation group showed only a slight advantage, it must be borne in mind that the chief value of insufflation is diagnostic.

A psychological effect was possible in all four groups, for, even in the "nothing done" group there was the factor of medical intervention, and these patients understood that they were receiving expert medical care. In order to consider further any psychological effect of medical intervention, one would have to compare the incidence of pregnancy in a group such as our bimanually examined patients with the incidence in a group of previously sterile but not medically attended patients. The sterility of an unattended group would either be inferred from childlessness or rest on answers to interrogation. On the other hand, the evidence for the previous sterility of sterility patients always includes the fact that they have found it necessary to seek medical advice. Thus, the two groups are not strictly comparable.

Even if one ignores the psychological factors, the difficulty of obtaining comparative figures regarding untreated sterile women remains; the best alternative is the study of a group such as the series of patients who were only bimanually examined. Some clinicians have concluded that pregnancy frequently soon follows bimanual examination of sterile patients; however, the method has not yet been adequately assessed. Whether or not this particular procedure proves worth continuing, the comparison of results is the best if not the only way to assess methods of treating sterility. The most important requirement for such comparisons is that the groups compared are large; the present communication is chiefly intended as a contribution to future compilations, extensive enough to minimize the effects of chance.

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In view of present knowledge, it appears advisable to combine diverse methods of treatment that appear relatively useful when employed separately. In view of the findings reported above, the combination of insufflation with hormone therapy deserves consideration. In this connection, one would welcome new preparations of hormones for oral administration, for these would do much to lessen the defaulting that has been noted among patients requiring repeated injections.

The intervention of chance in individual cases is well known, but I venture, in conclusion, to add a few instances of some salutary successes. In one case, a sound was passed in a 37-year-old woman, married five years. Insufflation was done eight months later. A cervical polyp was removed one year after insufflation. She became pregnant at the age of 40, a month after adopting a baby. In another case, an endometrial biopsy was performed in a 31-year-old woman, married three years. Two insufflations were done in the next two months. A sound was passed two years after the insufflations. A cervical erosion was cauterized a year later. She became pregnant two years after the cauterization. In a third case, a 31-year-old woman married six years had an insufflation. Endometrial biopsy was performed three years later and a sound was passed five months after that. Insufflation was repeated two years later. After no further treatment for two years, she became pregnant.

SUMMARY

A total of 1,575 primary sterility patients were followed for 12 months, 893 after insufflation, 253 after the passing of a uterine sound, 286 after bimanual examination, and 143 after commencing injections of progesterone combined with estradiol benzoate. The pregnancy rates at the end of three months were fairly uniform (6.9% to 8.4%); at the end of the year the rates were respectively 17.4, 17.8, 10.8, and 19.6%. Larger comparative compilations are required to ascertain the validity of the results.

REVIEW OF MASS CHEST X-RAY SURVEYS

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As the community-wide chest x-ray survey has developed in recent years, it has become, today more than ever, a concentrated attack on tuberculosis. Through the use of the photofluorograph, we now screen entire communities—the adult population of whole cities or large metropolitan areas—and, in so doing, find tuberculosis and gather the information we need to build more effective tuberculosis control.

In the achievement of these purposes, the community-wide chest x-ray survey is based on a blending together of the efforts of all the resources, skills, interests, and knowledge of an entire community. This blending together of resource and effort becomes apparent even before the photofluorographic units begin their screening operations. It becomes apparent in the modification of local tuberculosis control resources and practices to meet the special needs of the survey—in the provision of special laboratory services to aid the physician in the essential task of diagnosis, in the provision of special nursing and social work services in support of medical follow-up efforts, and in the expansion of treatment facilities to care for the cases found in the survey.

Out of the alloy of professional and public interest and effort that the community-wide survey represents, there has been forged in every locality where such programs have been undertaken an effective tool for tuberculosis case finding. The essence of the amalgam has been the leadership of the practicing physician and the medical society.

In the last four years, the United States Public Health Service has participated in 14 community-wide chest x-ray surveys. In so doing, it has aided in the small-film screening of nearly 5½ million persons from one end of the country to the other.

At the time that the Public Health Service made its decision to assist communities of over 100,000 population to conduct mass chest x-ray surveys, it was recognized that the x-ray had limitations as a diagnostic tool for tuberculosis. Some of these limitations stem from the variability of interpretation, while others arise from the variable patterns of the disease itself and from our lack of fully definitive knowledge of the disease process. As we know so well, a two-dimensional shadowgraph of the chest is not a perfect means for finding thoracic disease. Some infiltrates and, as a matter of fact, some cavities are subtle in appearance and difficult to distinguish. But the many unsuspected lesions that had been brought to light in limited mass surveys represented compelling reasons for enlarging the scope of tuberculosis case finding. The Public Health Service therefore embarked on its program to assist certain localities in x-raying persons over the age of 15.

At the same time, however, in an effort to cast some light on the question of the precise value of the mass survey to tuberculosis control—and to learn how to minimize the x-ray's limitations—the Public Health Service set up two research facilities to be conducted concurrently with actual mass survey operations. One of these, which was set up in Muscogee County, Georgia, was designed to study the occurrence and spread of tuberculosis within a community following an intensive case-finding program. The other, which was organized as the Central Cooperative Clinic in Philadelphia, aimed to follow the health histories of tuberculosis suspects found in industrial surveys. Both these research facilities had the over-all purpose of providing the knowledge for sharpening and refining mass survey operations.

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Although it was recognized at the outset that the findings in one community are not applicable to all communities, Muscogee County, which includes the city of Columbus, was selected as the over-all check-plot base for studying the effects of mass x-ray surveys. It is already apparent from this particular study—where, by the way, we now have survey information to correlate with tuberculin sensitivity findings and general tuberculosis mortality information—that the immediate effects of a chest x-ray survey may depend, to some extent, on the importance of endogenous disease that becomes active within a community after a screening program.

In the three and a half years following the initial screening program, average annual death rates appear to be about the same for both the group that received x-ray examinations and the group that did not. Superficially, then, it might seem that the survey had no effect on the death rate of those participating in the survey. But, if we assume that early detection, isolation, and treatment in tuberculosis do prevent death from the disease—an assumption that we must make if we are to have a basis for our control efforts then we must conclude that the survey did reach the more critical or more vulnerable portion of the population. Without the screening program, death rates for the group actually surveyed would perhaps have been higher.

Certainly, the prompt isolation of the infectious cases revealed by the x-ray survey must have had some effect on the spread of the disease by limiting the incidence of new exogenous infections and exogenous reinfections. The true effects of the x-ray survey and its follow-up may therefore be masked, to some extent, by the amount of silent and invisible endogenous disease that existed in the community. Obviously, the whole question of the relationship of exogenous and endogenous infections and their relative importance need elucidation before the exact value of a chest x-ray survey can be assayed.

Clarification of this enigma of the nature of tuberculosis might, perhaps, also shed some light on the occurrence of 25 postsurvey deaths among persons whose survey roentgenograms, even in retrospect and with knowledge of the exact location of the fatal lesions, were clearly and indisputably free of any indication of tuberculous disease. In this connection it is important to note that, of the 25 who died, 3 were white and 22 were Negro.

In the three and one-half years following the survey, the average annual tuberculosis death rate for the entire population was 34.0 per 100,000. For the white population it was 17.5 per 100,000, while for the Negroes it was 72.4. In contrast, the death rates for those with negative initial survey roentgenograms were 3 per 100,000 for whites, as against 39 for Negroes. In other words, the death rate for the Negroes was 13 times that for the whites. This, in spite of the fact that case finding coverage among the Negro population of Muscogee County was more nearly complete than among whites.

For the white population, the Muscogee County experience indicates that case finding and subsequent medical supervision appear to meet the problem of those who might otherwise die of tuberculosis. For the Negroes, however, it would appear that resurveys at frequent intervals—or, at least, more frequent and more intensive case finding of some sort—is highly desirable if they are to benefit by early discovery of the disease.

It must be admitted, however, that there is no clear indication of the best approach to the problem. Having identified the especially vulnerable group, should we address our subsequent case-finding efforts toward that specific group, or toward the entire population that contains that group? Continued analysis of information from such programs as the Muscogee County study, as well as those from the operating programs in the various cities themselves should provide the knowledge we need to answer this question and to increase the value of mass case finding as a tuberculosis control tool.

Detailed findings from the surveys in which we have participated are of interest as they relate to the coverage they achieve and the amount of disease they bring to light. In the first stage of survey operations—that is, the small-film screening examination—coverage in the 14 community-wide programs to date has varied from place to place. The goal of screening operations is usually set at 80% of the eligible population 15 years of age and over. In actual operations, total small films taken range between 55% of this eligible population (in St. Paul, Minn.) and 93% (in Salt Lake City).

Generally, the two sexes respond more or less equally. Response by race, however, is varied from one city to another—in Denver, screening coverage for nonwhites was far below that for the white population. There, 42% of the Latin-American population and 61% of the Negroes were screened, as against 77% of the white population. In Washington, D. C., on the other hand, both whites and nonwhites had more or less equal coverage.

It has been our experience that the older age groups do not usually respond to small-film operations as well as the younger population groups. In the Seattle survey, which was held in 1948, the response ranged from a high of 84.2% in the 15-24 year age group to a low of 35.8% for those 65 years of age and over. Similarly, in the Cleveland survey (1949) coverage ranged from 74.5% in the 15-24 age group to 35.3% for persons 65 and over. These percentage-coverage figures represent, at this time, the usual range of expectancy for small-film screening programs.

In the second stage of survey operations—confirmatory 14 by 17 inch films for those with suspicious small-film findings—our experience has been as follows: First, we have found that between 2% and 7% of those screened by small-film examination will need confirmatory 14 by 17 inch films. Of those recalled for confirmatory films, between 80% and 95% have actually responded.

Of the total number of 14 by 17 inch films taken in the 14 community-wide surveys to date, the total prevalence of findings suspicious of tuberculosis have ranged from 0.6% of all persons receiving small-film examinations (for Salt Lake City) to 2% (for Maricopa County, Arizona, preliminary information). In two surveys, Seattle and Cleveland, the prevalence of 14 by 17 inch film findings suspicious of tuberculosis were tabulated by census tract, as a means of indicating the correlation between these findings and socioeconomic status. The information appears to confirm the commonly held notion that tuber-

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culosis prevails to a greater extent at the lower socioeconomic levels. In Seattle, the lowest "income" group experienced a prevalence rate of 13.7 suspicious large films per 1,000 persons examined, while the highest level showed a rate of 10.7 per 1,000. In Cleveland, the same general pattern is apparent, with a rate of 9.2 per 1,000 for the lowest economic level and 6.2 for the highest.

In most surveys, referral to private physicians or public clinics occurs immediately after the confirmatory large films are taken and read. In some, however, further diagnostic study is undertaken before a referral is made. This was the case in the Denver survey, where a diagnostic center was established as part of the survey organization in an effort to furnish the practicing physician to whom the patient was to be referred with as much pertinent diagnostic information as possible. The Center was staffed by local physicians, and patient referrals were made after the tentative diagnostic study indicated the need for long-term supervision.

In all of the surveys, suspects are referred to private physicians of their own choice or to public clinics, depending, in general, on their ability to pay for medical care. To date, referrals have been made to private physicians for about 80% of the suspects found, while some 20% have been referred to public clinics. In the Denver survey, 73% of all tuberculosis cases—including active, inactive, and questionably active—were sent to private physicians, while 23% were sent to public clinics. For those with active tuberculosis, the proportion choosing clinic follow-up was higher.

Since the principal aim of mass chest x-ray surveys is to find significant tuberculosis in the screened population, the question of how much active tuberculosis is found is fundamental. Although reporting by private physicians has not been complete, or diagnostic methods and criteria uniform, the information we have assembled indicates that about one out of every 1,000 persons screened will have active tuberculosis that is clinically recognizable. Our experience indicates, too, that many of those found with inactive and questionably active disease will later prove to have definitely active tuberculosis.

Moreover, as we have found from a detailed analysis of five surveys, about 85% to 90% of the active cases are unknown to the health department. The identification of these previously unknown cases of active tuberculosis represents one of the major contributions of the community-wide survey wherever it is held.

Although tuberculosis is the primary concern of community-wide chest x-ray surveys, the screening programs do identify other pathological conditions of the chest, including thoracic neoplasms and cardiovascular abnormalities. In view of our aging population, this is assuming greater value as a by-product of tuberculosis case-finding projects. In the Boston survey, which was held in the latter part of 1949, special procedures were instituted for the follow-up of tumor suspects found in the screening program. A roentgenologic review board was organized to read the 14 by 17 inch chest x-rays and to identify all findings suggestive of thoracic neoplasms. After the radiological interpretations, all suspects were referred to a medical social worker for help in obtaining medical follow-up either under the supervision of private physicians in the area or in public clinics. According to Dr. C. L. Scamman, a total of 76 cancer neoplasms were found, of which 43, or well over half, were of the primary type. Furthermore, most of the cancers found were discovered at a time when they were most likely to be resectable.

For the 43 cases of proved primary cancer, the total time required to identify them—an all-important factor in their control—was relatively brief. As a matter of fact, the total time that elapsed between the time the small film was taken and the establishment of a final diagnosis averaged approximately 56 days.

As one would expect, the Boston survey found a direct correlation between the prevalence of cancer and age. Except for the oldest age group examined—where incidentally, the number of persons screened was extremely low—the total number of cancer cases found was greater in each successive age group. As one would expect, too, more neoplasms were found among men than among women.

In this same survey in Boston, special procedures were also established to identify the cases of cardiovascular abnormalities among the population screened. Observations on this subject are now undergoing intensive analysis, and findings will be published in the near future. In our experience, readings of cardiac abnormalities have appeared in 2 to 10 x-rays of every 1,000 taken in community-wide surveys. Since information on the follow-up of cardiac suspects is scanty, it is difficult to estimate the effects of the identification of those with possible cardiovascular disease. There are rather divergent views regarding the value of the x-ray in finding cardiovascular disease that can be benefited medically. Findings from the special study in Boston, it is hoped, will help to resolve these divergent views.

Just as the Boston survey has made cancer and heart disease studies possible, so does every community-wide survey provide the opportunity for studying tuberculosis and tuberculosis control efforts. In some areas, physicians to whom suspect cases have been referred have done a thorough job of diagnostic study and patient follow-up and have reported back to the survey organization consistently and in detail. Wherever this has occurred—where physicians have conducted complete follow-up on all referred suspect cases and have reported to the survey organization—the structure of knowledge about tuberculosis is being built up and control programs are being modified to conform with the knowledge gained. With the survey's stimulus and the increase of public interest in and support for tuberculosis control, improvements in the program have been made possible in many places.

In Denver, for example, several tuberculosis control program improvements can be directly attributed to the impact of the community-wide survey. First, more funds are now available for the care of tuberculosis patients—to the extent of about 50%. Personnel has been increased, photofluorographic equipment has been purchased, and the entire, official control program has been expanded.

In Salt Lake City, the survey brought with it a tuberculosis case register, a device that had not existed there prior to the survey. In Seattle, hospitalization of tuberculosis patients rose to 4.3 patients per annual death.

CONCLUSION

In our experience with community-wide chest x-ray surveys, over the past four years, we have learned, that, despite the x-ray's limitations, the mass survey has positive value in the discovery and consequent control of tuberculosis. As our research programs in mass radiography—and our operating programs—progress in the future, we can expect that the mass approach to tuberculosis case finding will make even greater contributions to the fight against tuberculosis in the United States.

TREATMENT OF PULMONARY ACTINOMYCOSIS WITH CHLORAMPHENICOL

REPORT OF A CASE

Maxwell L. Littman, M.D., Ph.D., New York, Lieutenant Colonel John S. Paul (MC), United States Army
and
Matthew H. Fusillo, B.S., Washington, D. C.

Actinomycosis was first described in the cervicofacial form in cattle by Bollinger [1] in 1877. His botanical colleague, Harz,[2] observed the radiate formation of the micro-organism, and applying the term "actinomyces" from the Greek to connote "ray-fungus," named the disease "actinomycosis." It was not until the following year, however, that the first case of actinomycosis in a human being was reported by Israël.[3] By 1885 he had accumulated data on 38 cases, and had written the first comprehensive, clinical description of the disease in man.[4] Together with Wolff [5] in 1891, he described the etiologic agent and its anaerobic growth in detail.

Until the appearance of the sixth edition of "Bergey's Manual of Determinative Bacteriology" [6] in 1948, numerous investigators held the opinion that actinomycosis in cattle and man was caused by the same anaerobic micro-organism, and, depending on the investigator, called it either Actinomyces bovis or Actinomyces israeli. The former statement appeared as fact in the latest editions of textbooks of bacteriology and mycology. Presumably based on the work of Erikson,[7] "Bergey's Manual" catalogues Actinomyces israeli as the cause of actinomycosis in human beings, and Actinomyces bovis as the etiologic agent of the bovine disease. Erikson's opinion that there are two distinct cultural types of anaerobic Actinomyces was amply supported in 1949 by the work of Thompson [8] at the Mayo Clinic.

Through the efforts of numerous investigators, such as Wolff, Israël, Sullivan, Goldsworthy, Lord, Naeslund, Emmons, Slack, and Rosebury, it has been established clearly that the anaerobic Actinomyces is a frequent, if not normal, inhabitant of the oral cavity and respiratory tract and rarely is found as a free saprophyte. Infection in man is endogenous in origin, therefore, rather than exogenous, as has been the popular belief for many years.

The disease is usually initiated by the disruption of the normal barriers to infection by trauma or following a disease process. Thus, cervicofacial actinomycosis may follow tooth extraction, periodontitis, or severe dental caries; while abdominal actinomycosis may appear several weeks or months after an acute, perforative gastrointestinal disease, such as acute appendicitis, perforated colonic diverticulum, perforated peptic ulcer, acute ulcerative disease of the intestinal tract, or after trauma.[9] Pulmonary actinomycosis is likely to appear in persons with poor dental hygiene following aspiration of actinomycetes-infected material from the mouth, since these organisms are normally harbored in great numbers in pyorrheic gums, carious teeth, and tonsils. Actinomycotic pneumonia may result, with pleural invasion and the ultimate formation of multiple, draining thoracic sinuses which are extremely difficult to treat and to eradicate. It is also realized now that actinomycosis in its various forms is as common in urban as in rural areas.[9a]

Although numerous forms of therapy have been employed successfully for cervicofacial actinomycosis, these have proved to be of less value in the management of the more grave pulmonary and abdominal forms. Some of the therapeutic agents have been iodides, copper or iron salts, gold preparations, thymol, arsphenamine, vaccines, and radiation. Surgical treatment has consisted of repeated excision and curettage. With the introduction of sulfadiazine for actinomycosis in 1937,[10] and penicillin in 1943,[11] a new therapeutic era for this disease was opened and the prognosis was vastly improved. By 1948 penicillin therapy for actinomycosis was firmly estab-

Miss Marian Schoenherr assisted in some phases of the laboratory work.

From the Thoracic Surgical Section and Laboratory Service of Walter Reed Army Hospital.

Some of the illustrations have been omitted from THE JOURNAL; they will appear in the authors' reprints.

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lished.[12] In 1950 aureomycin was added to the armamentarium by McVay and co-workers,[13] who successfully treated one case of cervicofacial actinomycosis with this antibiotic.

Meanwhile, chloramphenicol (chloromycetin®) was discovered in 1947,[14] and its antibiotic activity demonstrated. Then in 1949, McLean and co-workers,[15] studying the in vitro susceptibility to chloramphenicol of a large variety of micro-organisms, noted that one strain of Actinomyces bovis was inhibited by 5 γ per milliliter. We extended this observation to Actinomyces israeli the following year,[16] and we discovered that six strains of the micro-organism, all isolated from patients with actinomycosis, were inhibited in vitro by concentrations of antibiotic ranging from 1 to 3 γ per milliliter. On the basis of this marked in vitro sensitivity, a clinical trial of chloramphenicol in the treatment of actinomycosis was recommended.

REPORT OF A CASE

W. P., a white man aged 46, had increasing difficulty with pyorrhea and abscesses of the gums in 1948 and 1949, necessitating extraction of four upper canine and incisor teeth in July, 1950. In October he began to experience intermittent sharp, right upper abdominal pain, unrelated to food intake, which radiated around to the back and up to the right scapula, and, in addition, pain in the right chest at the level of the fourth anterior rib. He became moderately dyspneic and produced a foul-tasting but scanty greenish-yellow sputum. Since treatment in his locality for cholecystitis had been unsuccessful, the patient sought hospitalization at Walter Reed Army Hospital, where initial roentgenograms of the chest were interpreted as marked enlargement of the right side of the heart. Shortly afterward, he expectorated large quantities of foul-smelling greenish-yellow sputum. Subsequent chest fluoroscopy and roentgenograms showed the "cardiac enlargement" to be a partially emptied cyst, located in the right, medial posterior lung field and probably within pulmonary tissue (Fig. 1). At operation two months later, however, the remains of the "cyst" proved to be a localized, loculated empyema cavity contained entirely within the pleural space and not encroaching on pulmonary parenchyma.

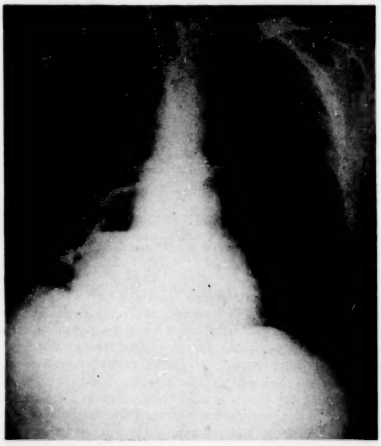

Fig. 1.—Roentgenogram of chest taken Nov. 13, 1950, reveals a loculated, localized actinomycotic empyema cavity, of an estimated capacity of 350 cc., within the right lung.

Physical examination revealed a tall, chronically ill, white man with a temperature of 102 F. A blood pressure of 133 systolic and 82 diastolic, a pulse rate 82 per minute, and a respiratory rate of 18 per minute, who had exceedingly foul breath, pyorrhea alveolaris, severe dental caries and periodontoclasia, cheilosis of the oral commissures and a smooth red tongue indicative of nutritional deficiencies, a slightly enlarged liver but no abdominal tenderness, lungs which were clear to auscultation and percussion, and occasional premature auricular beats but no enlargement of the heart by percussion.

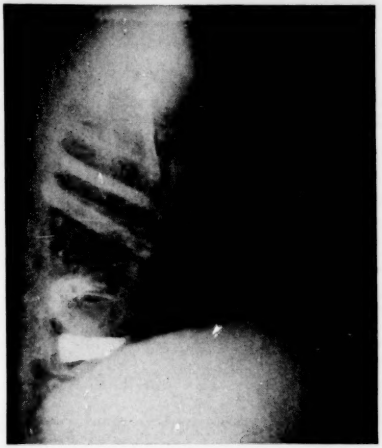

Fig. 2.—Lateral roentgenogram demonstrates the size and extent of lipiodol®-injected empyema cavity.

On the day of admission, Nov. 18, 1950, the empyema cavity was aspirated through the eighth right posterior intercostal space, yielding 300 cc. of thick, extremely foul-smelling, greenish yellow pus, microscopic examination of which showed masses of gram-positive, non-acid-fast, slender, branching rods resembling Actinomyces, gram-positive streptococci, and fusiform bacilli. Cultivation of the pus yielded Actinomyces israeli, anaerobic streptococci, and anaerobic fusiform bacilli. No aerobic organisms were recoverable from this foul material. Lipiodol® (an iodized oil used as a contrast medium) instilled into the cavity appeared on chest roentgenogram behind the right leaf of the diaphragm but not involving it and extending low into the posterior portion of the lung field (Fig. 2). The patient tasted lipiodol® shortly afterward, indicating the presence of a bronchopleural fistula. The strain of Actinomyces isolated was sensitive to 3 γ chloramphenicol per milliliter which was within the "very sensitive" range reported for six other pathogenic strains,[16] while the anaerobic Streptococcus was sensitive to 1 γ per milliliter.

The white blood cell count was 16,200 per cubic millimeter, with a differential cell count of 89% polymorphonuclear leucocytes, 9% lymphocytes, and 2% monocytes. The red blood cell

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count was 5 million per cubic millimeter, and the hemoglobin value was 13.9 gm. Prothrombin time was 16 seconds, the normal laboratory base line for this and subsequent determinations being 15 to 16 seconds. The sedimentation rate (Wintrobe) was 30 mm. in 60 minutes, corrected. Blood urea nitrogen was 15 mg. per 100 cc.; total serum protein, 6.4 gm. per 100 cc.; serum albumin, 2.9 gm.; and serum globulin, 3.5 gm. The urine was

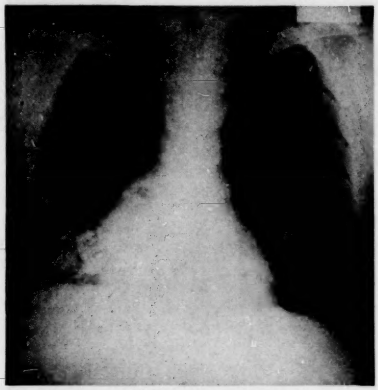

Fig. 3.—Roentgenogram of chest taken Nov. 24, 1950, after six days of chloramphenicol therapy demonstrates reduction in the size of the cavity.

essentially normal. Coccidioidin 1:100, blastomycin 1:100, histoplasmin 1:100, and first and second strength intradermal tuberculin tests (purified protein derivative) were negative.

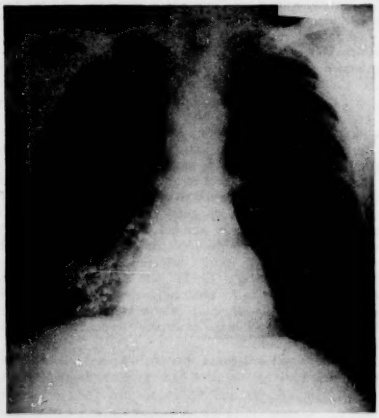

Fig. 4.—Roentgenogram of chest taken Dec. 28, 1950, following 40 days of continuous chloramphenicol therapy and two local instillations of crystalline antibiotic reveals obliteration of the empyema cavity and the presence of residual Lipiodol.®

Chloramphenicol therapy was instituted in doses of 750 mg. orally every four hours, supplemented by two successive instillations into the empyema cavity of 2 gm. of sterile crystalline chloramphenicol (supplied by Parke, Davis & Co., Detroit, Mich.), suspended in 10 ml. of isotonic saline. Daily intramuscular injections of vitamin B complex, oral multivitamins, and a high protein, high caloric diet were prescribed. The patient's temperature returned to normal by the fourth day of therapy, and the contents of the empyema cavity were reduced in volume to 65 cc. of thin, nonodorous, sterile material at the third aspiration (Fig. 3). The fifth and all subsequent attempts at thoracentesis failed to yield any pus. Serial roentgenograms of the chest demonstrated progressive diminution of the size of the cavity until Dec. 28, 1950, when the right lung field was entirely clear, save for residual lipiodol® in the pleural space (Fig. 4). The patient was referred to the dental clinic, where eradication of focuses of infection was recommended. All of the patient's teeth were then removed while he continued to receive chloramphenicol. Cultivation of the scrapings of the extracted teeth yielded Actinomyces israeli, as well as many other mouth organisms. The patient was given a short convalescent leave, during which time the oral daily dose of chloramphenicol was reduced to 2 gm. (Fig. 5).

On Jan. 10, 1951, after 53 days of continuous chloramphenicol therapy, a right thoracotomy was performed with the patient under gas-oxygen-ether anesthesia with resection of the seventh

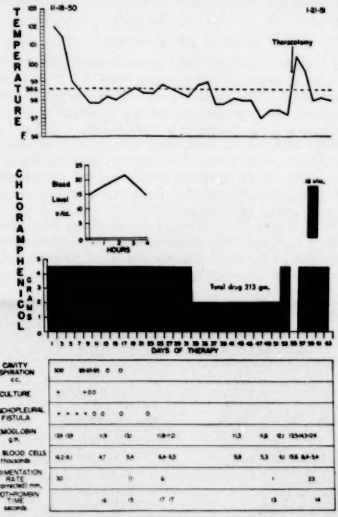

Fig. 5.—Chart showing response of a man aged 46, who weighed 182 lb. (82.7 kg.) and who had actinomycotic empyema of the right lung, to chloramphenicol.

rib. When the chest was opened, the right lung was completely adherent to the chest wall by filmy, easily separable adhesions, and in the posterior gutter, at the level of the eighth, ninth, and tenth ribs, by dense adhesions, the latter representing the remains of the actinomycotic empyema cavity as seen in chest roentgenograms (Fig. 1 to 4). The lung was freed from the chest wall, except in this firmly attached area. Extrapleural resection was elected as the procedure of choice. The encapsulated cavity, measuring 5 by 3 cm. and containing 4 to 5 cc. of thick, yellowish, nonodorous fluid which later proved to be sterile, was removed from the lung and chest wall by sharp dissection. Upon reinflation of the lung, several tiny air leaks which appeared on the posterior surface of the right lower lobe were closed by absorbable gelatin sponge (gelfoam®) placed between it and the parietal pleura. A posterior drain was placed in position, and the chest was closed in layers in the usual manner. The patient tolerated the procedure well.

Pathological examination of the cavity wall revealed highly vascular granulomatous tissue, areas of suppuration and fibrosis, microabscesses, and giant cells, a tissue reaction compatible

with that of actinomycosis. Several granules were seen in various sections but they did not contain any branching organisms.

The patient's postoperative course was uneventful, and he was discharged on the 10th postoperative day with a completely reexpanded clear right lung, asymptomatic and afebrile (Fig. 6). A letter from him in May stated that he was in good health.

BACTERIOLOGY

The traditional and cumbersome technique of deep veal infusion agar cultivation for the isolation of pathogenic anaerobic actinomycetes as recommended in many standard textbooks is unnecessary, since the micro-organism grows readily in surface colonies on suitable agar medium, and may therefore be isolated in the pure form by simple bacteriologic techniques.

Actinomycotic exudates are streaked over (1) several bacto® brain-heart infusion agar plates containing 0.5% dextrose and planted into (2) thioglycollate glucose broth (Brewer's anaerobic medium). The plates are incubated for four to six days at 37 C. in a Brewer anaerobic jar with 5 to 10% added CO_2. Although many bacterial species thrive under anaerobiosis on the brain-heart infusion dextrose agar, colonies of Actinomyces israeli are so distinctive that, with a little experience, one may easily detect their presence. They are tiny, only 1 to 3 mm. in size, and appear starchy white, although some strains are slightly yellow or greyish. The surface of the colony glistens under reflected illumination and has an irregular and contoured surface very much like the crown of a molar tooth.[17] The colony is adherent to the agar and is difficult to emulsify, often coming away from it in one piece and leaving a pitted

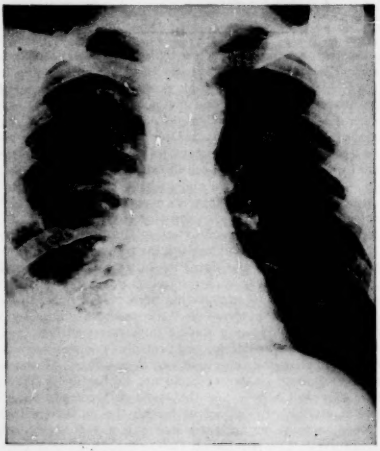

Fig. 6.—Roentgenogram of chest taken Jan. 19, 1951, nine days postoperative, reveals a missing seventh right rib, some elevation of the right diaphragm, residual lipiodol, * and some pleural thickening, but essentially clear lung fields.

area. Microscopic examination reveals a loose aggregate of branched gram-positive, non-acid-fast, long slender rods (Fig. 7).

Colonies of Actinomyces bovis under anaerobiosis on the same agar medium vary in size from 1 to 2 mm., are also starchy white, but do not have the roughened appearance of Actinomyces israeli, and are considerably easier to emulsify. Furthermore, pure culture growth of the micro-organism in thioglycollate medium is diffuse, while that of the human pathogen is discrete, in the form of compact granules, irregularly round and

Fig. 7.—Actinomyces israeli, gram stain, × 1,400.

of variable size, usually found below the oxygenated zone of the medium.

Primary tubes of thioglycollate medium are incubated four to seven days at 37 C., and finely drawn Pasteur pipettes are employed to fish out suspicious colonies of micro-organisms. These are streaked over bacto® brain-heart infusion dextrose agar and placed under anaerobiosis with added CO_2. Although pathogenic, anaerobic actinomycetes grow in liquid thioglycollate medium at a rate slower than those of the usual ubiquitous secondary micro-organisms; they appear in sufficient numbers in four to seven days to permit their isolation in pure culture. Other organisms besides Actinomyces israeli which form balls or colonies in liquid thioglycollate medium are various species of anaerobic streptococci.

Pure strains of pathogenic, anaerobic actinomyces isolated by one of us (M. L. L.) in the past from various patients with actinomycosis required either limited oxygen atmosphere in anaerobic jar or reduced oxygen tension in thioglycollate medium and have consistently failed to grow aerobically. This coincides with the experience of other workers.[18] Although a small percentage of strains of actinomyces are reported to be capable of scant

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growth under aerobiosis,[19] the majority thrive best under anaerobic or microaerophilic states.

Pathogenic anaerobic actinomycetes are to be differentiated from the aerobic Nocardia asteroides, a pathogenic, partially acid-fast, gram-positive, branching rod which does not produce the typical actinomycotic granule in tissue and is the agent of nocardiosis, a tuberculosis-like disease of high mortality. The confusion in the nomenclature of the etiologic agents of actinomycosis and nocardiosis was clarified in 1943 by Waksman and Henrici.[20] Nocardia asteroides, growing aerobically on brain-heart infusion dextrose agar, produces small, orange-yellow colonies, the surface of which becomes powdery with age owing to fragmentation of the mycelium into rod-shaped conidia.

Actinomyces bovis may be confused easily with anaerobic or microaerophilic diphtheroids. However, the latter organisms are, for the most part, nonpathogenic to mice on intraperitoneal inoculation with mucin,[21] or, if pathogenic, they fail to produce the typical actinomycotic tissue lesion. They grow much more rapidly than actinomycetes in both fluid thioglycollate medium and anaerobic brain-heart infusion dextrose agar, visible growth appearing within 24 to 48 hours, diffusely in thioglycollate medium, and in greyish, butyrous, easily emulsifiable colonies in the latter medium.

In vitro sensitivity of Actinomyces israeli to chloramphenical was determined by the method of Littman, Phillips, and Fusillo,[16] while serum chloramphenicol levels were assayed by the technique of Smith, Landers, and Forgacs.[22] Plates of thioglycollate agar seeded with 400,000 spores per milliliter of Bacillus subtilis received 4 small metal cylinders containing patient's serum. After incubation of the plates, cleared zones produced by the patient's serum were compared with those obtained with standard concentrations of chloramphenicol and the level computed.

COMMENT

The favorable response of only one patient to chloramphenicol therapy could hardly be used as a basis for a conclusive statement concerning the clinical effectiveness of this antibiotic for pulmonary actinomycosis. It does, however, serve to point out that additional clinical evaluation of chloramphenicol for this and other forms of actinomycosis is worthwhile, especially when reports exist of the inadequacy of combined penicillin and sulfadiazine therapy for permanent cure of some patients with pulmonary actinomycosis,[23] and the inadequacy of penicillin in controlling anaerobic streptococci which frequently coexist with actinomycetes in pulmonary lesions. It also demonstrated to us the feasibility of instilling crystalline chloramphenicol into an empyema cavity with apparent minimal reaction.

Because of the chronicity of pulmonary actinomycosis, which is characterized by periods of remission and exacerbation, a prolonged period of chloramphenicol therapy was thought to be necessary, as is customary with penicillin and sulfadiazine treatment. The patient received a total of 213 gm. of chloramphenicol in continuous therapeutic doses over a period of 64 days. Although a relative neutropenia and lymphocytosis developed, neither leucopenia nor anemia resulted from the therapy, as reported in three patients by Volini and co-workers[24] (Fig. 5). Rib bone marrow obtained at operation on the 53rd day of chloramphenicol treatment revealed no evidence of maturation arrest of either erythroid or granulocyte series. Prothrombin levels were normal throughout the period of therapy. In another patient with a branchial cyst, not reported on here, who received 260 gm. of chloramphenicol over a period of 56 days, leucopenia or anemia did not develop.

SUMMARY AND CONCLUSIONS

Chloramphenicol (chloromycetin®) was successfully employed for the treatment of one case of pulmonary actinomycotic empyema caused by Actinomyces israeli. This antibiotic administered daily in therapeutic doses over a period of two months caused no appreciable hemopoietic change in two patients.

New York Medical College, Flower and Fifth Avenue Hospitals, New York (Dr. Littman).

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The Ancient Art of Feeling the Pulse.—The Ars Sphygmica or ancient science of the pulse dates back into antiquity to long before Galen's time. It is probable that Chinese and Hindu physicians were skilled in feeling the pulse before the dawn of Hippocratic Medicine, and Oriental pulse-lore appears to have developed quite independently of Greek influence. . . . According to legend, Chinese sphygmology was founded by the Emperor Hoamti who is said to have been the author of several books on the pulse about 2500 B. C., and to have been very skilled in the art. . . . The Chinese physician visited his patients in the morning, before taking food, when free from all cares and distractions, and he was enjoined to banish all other thoughts from his mind in order to concentrate on the pulse. This was important because the pulse was timed by the respiration of the physician, four pulsations to each respiration being the natural rate in adults. The patient's arm having been placed on a cushion, the pulse was then palpated at three separate places by the physician's index, ring and middle fingers respectively. . . . At each site, light, moderate, and firm pressure was applied in turn so as to elicit the superficial and deep pulses. All the permutations of these six pulses could not be hastily interpreted, and we may well believe that the whole performance occupied several hours. . . . The art of feeling the pulse was highly developed amongst the ancient Hindu physicians. . . . Susruta (5th century A. D.), the Indian Galen, though most renowned for his surgery, is depicted feeling the pulse. . . . Like the Chinese, the Hindus laid great stress on not only the patient but also the physician being at ease. . . . The pulse was felt at the wrist, on the right side in males and on the left side in females; in the case of eunuchs a nice discretion was necessary in selecting the appropriate side. . . . Before the discovery of the circulation, no rational basis existed for understanding the pulse; it was only possible to describe what the finger felt and to interpret this empirically in terms of the primitive medical ideas of the time.—D. Evan Bedford, The Ancient Art of Feeling the Pulse, *British Heart Journal*, October, 1951.

PRIMARY CEREBRAL THROMBOPHLEBITIS

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Thrombophlebitis may be primary or secondary. The latter form occurs in conditions known to be associated with thrombosis of veins such as childbirth, arthritis, infectious diseases, malignant tumors, recent operations, and blood dyscrasias. The primary form is of unknown cause and is often termed recurrent thrombophlebitis or thrombophlebitis migrans. The vessels affected are principally the superficial veins of the upper and lower extremities, although involvement of the visceral veins is not uncommon. Recurrent primary thrombophlebitis of the cerebral veins has been suspected clinically, but a description of the clinical as well as the gross and microscopic changes of such a case has not been recorded in the literature. For this reason the present case is of interest.

REPORT OF A CASE

The patient was a white Jewish man, 52 years, who was well until one week before admission to the hospital, when he noted fatigue and a dull frontal headache. These symptoms persisted, and two days before entering the hospital the patient experienced a generalized convulsion of Jacksonian type, beginning in the left hand, which was followed by a sharp increase in the severity of the headache. Two similar convulsions occurred on the day before hospitalization.

Six years previously the patient had experienced short periods of dizziness that subsided gradually. He was then well until 10 months before admission to the hospital, when short episodes of dizziness recurred. The attacks of vertigo were associated with occipital headache. The patient was hospitalized; physical examination was normal except for symmetrically diminished deep tendon reflexes. The cerebrospinal fluid was normal, and x-rays of the skull were not remarkable. He had been smoking one package of cigarets daily, and this was stopped. A diagnosis of vasospastic disease of the right side of the cerebrum was made, and the patient was dismissed from the hospital after five days. During the 10 months before his final hospitalization the patient had occasional pain in the lower legs. The pain was brought on by exertion. On several occasions he had a low grade fever that subsided spontaneously.

On admission his temperature was 97.6 F, pulse rate 76, respirations 22, and blood pressure 142/82 mm. Hg. The patient was well nourished and somewhat lethargic and did not appear acutely ill. Results of physical examination of the head, chest, and abdomen were not remarkable. The feet were cold and slightly cyanotic, became dark bluish red when dependent, and blanched quickly on elevation. The dorsalis pedis pulses were absent in both feet. Neurologic examination revealed normal pupillary and conjunctival reflexes. Extraocular movements were normal, the visual fields were not diminshed, and results of fundoscopic examination were normal. The function of all cranial nerves was intact. The deep tendon reflexes were markedly diminished in both lower extremities and in the left upper extremity. The superficial reflexes were normal except for a diminished left cremasteric reflex. No pathologic reflexes were elicited. Pain perception was normal. The heel-to-knee and finger-to-nose tests were performed with difficulty on both sides and particularly on the left. Slight weakness and reduced stereognosis were elicited in the left hand. Muscle strength elsewhere was normal.

Urinalysis disclosed no abnormalities. Hematologic examination revealed 13.5 gm. of hemoglobin per 100 cc., 4,310,000 erythrocytes, and 10,000 leukocytes per cubic millimeter, with a normal differential count and a negative Kahn reaction. Lumbar puncture showed clear spinal fluid and pressure 290 mm. of water; responses to venous compression revealed no subarachnoid block. A sample of fluid was not removed. X-rays of the skull were normal. The electroencephalogram disclosed waves of low frequency with highest amplitudes from the right frontal and right parietal leads. Injection of radioisotopes revealed no focal concentration of the dye. The ventricular fluid was clear, and examination revealed 21 mg. of protein per 100 cc. and no cells. After injection of air into the ventricles, x-rays disclosed nondeviated midline structures with slight depression of the right lateral ventricle with failure to visualize the right posterior horn. These changes were interpreted as suggestive of a right occipital lobe tumor.

The patient became confused, and on the ninth hospital day a flaccid paralysis of the left side developed. Two days later a right parietal craniotomy was performed; a focus of soft bulging cortex, 5 cm. in diameter, was encountered over the posterior parietal region near the vertex. In this region the cerebral veins were thrombosed. A narrow margin of thickened pale yellow adherent arachnoid extended along the side of each thrombosed vein. The arteries were stated to appear unusually small. A similar region of venous thrombosis, 4 cm. in diameter, was present over the midportion of the right frontal lobe. Incision of the soft parietal cortex revealed a subcortical hematoma, 3 cm. in diameter, that was evacuated. The defect was filled with fibrin foam, the bone was not replaced, the dura was left partially open, and the skin incision was closed. The patient appeared in good condition immediately after the operation but died suddenly on the first postoperative day

AUTOPSY

The brain weighed 1,350 gm. The gyri were flat, and the sulci were narrow over both cerebral hemispheres. Recent subarachnoid hemorrhage was present about an incision in the right posterior parietal region that measured 5 cm. in length. Portions of the veins of the right frontal and both parietal lobes were distended and firm and revealed on each side a narrow margin of pale gray, slightly thickened arachnoid. The surface of the left frontal lobe, both occipital lobes, and the cerebellum, pons, and medulla appeared normal. The arteries of the circle of Willis revealed slight arteriosclerosis. Coronal sections of the cerebrum disclosed a defect in the white matter of the right parietal lobe, measuring 5.5 cm. in diameter, that was filled with gelatine sponge and clotted blood (Fig. 1). This communicated with the surface through the recent incision of the cortex. The cavity lining was shaggy and dark red, and the adjacent white matter disclosed numerous foci of recent hemorrhage. Further coronal sections revealed separate foci of recent hemorrhage, measuring 2 to 20 mm. in diameter, that were present in the right parietal and occipital lobes, the left posterior parietal lobe, and the corpus callosum. A single focus of recent hemorrhage was also present in the midthoracic portion of the spinal cord. The cut surfaces of the midbrain, pons, cerebellum, and medulla were not remarkable. The cerebral ventricles were of usual contour and were lined by smooth, pale gray ependyma.

The heart weighed 375 gm. and was not unusual except for petechiae of the epicardium and a minute focus of dark red discoloration in the wall of the main left coronary artery. There was slight arteriosclerosis of the aorta. An easily detached soft mural thrombus, measuring 1.5 cm. in length, slightly encroached on the lumen of the right common iliac artery. The right and left lungs weighed 375 and 420 gm., respectively, and disclosed slight chronic pulmonary emphysema. The larger bronchi contained scattered plugs of viscid mucus. The liver weighed 2,000 gm. and was not remarkable except for slight chronic passive hyperemia. The kidneys weighed 175 gm. each. The surfaces revealed a diffuse and fine granularity. A bulging focus of dark red discoloration was present over the surface of the right kidney, which extended 1.7 cm. into the parenchyma. The right renal artery and its branches were grossly normal. The remain-

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This article has been abbreviated by the omission of Figures 3, 4, and 5. These will appear in the author's reprints.

ing structures, including the paranasal sinuses, were not unusual. The femoral and popliteal vessels were not examined.

Microscopic examination of the left frontal and both parietal lobes of the cerebral cortex revealed large distended veins occluded by recent thrombi (Fig. 2). The vein walls, thrombi, and perivenous arachnoidal spaces were densely infiltrated with polymorphonuclear leukocytes. Old or organizing venous thrombi were not seen in any section. In all other regions the meninges were normal and the vessels were patent. Arteries were distinguished from veins with elastic stains, and the arteries of the brain and meninges were normal except for slight arteriosclerosis in all sections examined. There were many foci of recent hemorrhage throughout the white and gray matter of the cerebrum, and these were frequently ring-shaped about minute central vessels. The cerebral tissue at the margin of the evacuated hematoma revealed focal necrosis, extensive recent hemorrhage and infiltration with mononuclear phagocytes containing blood pigment, and a few polymorphonuclear leukocytes. Sections of the midbrain, pons, cerebellum, and medulla were not remarkable. A single small focus of recent hemorrhage was present in the midthoracic portion of the spinal cord. However, an associated vascular lesion was not identified and the arachnoid vessels of the spinal cord were not remarkable.

Sections of the left main coronary artery revealed slight arteriosclerosis and a minute focus of recent and canalized hemorrhage within the media. Sections of the right common iliac artery revealed a loosely adherent recent mural thrombus. The subjacent arterial wall was infiltrated with lymphocytes, and the vasa vasora were dilated. There was focal necrosis of the right kidney as well as slight arteriolar nephrosclerosis of both kidneys. An occlusion of the right renal artery or its branches was not found. There was moderate reticular hyperplasia of the spleen and slight passive hyperemia of the lungs and liver. Results of microscopic examination of the myocardium, adrenals, prostate, testes, thyroid, pituitary, skin, and skeletal muscle were not remarkable.

The significant anatomic diagnoses included acute thrombophlebitis of the left frontal and the right and left parietal lobes of the cerebrum with recent hemorrhages of the cerebrum and spinal cord. There was slight arteriosclerosis and focal recent and canalized hemorrhage of the left main coronary artery, arteriosclerosis and slight chronic inflammation of the right common iliac artery with recent mural thrombus, and a recent infarct of the right kidney. In addition, the lungs and liver revealed slight chronic passive hyperemia.

Fig. 1.—Coronal section of cerebrum showing recent hemorrhages, site of evacuated hematoma, and thrombosed cerebral vessels at *A* and *B*.

Comment.—Examination of the cerebral vessels and brain revealed only recent thrombosis and acute inflammation of the veins. However, the clinical manifestations of cerebral involvement during the six years before death indicated that the thrombophlebitis was probably recurrent. The cerebral arteries were normal except for slight arteriosclerosis. Lesions of extracranial vessels were found only in the left coronary and right common iliac arteries. The changes of recent and old intramural

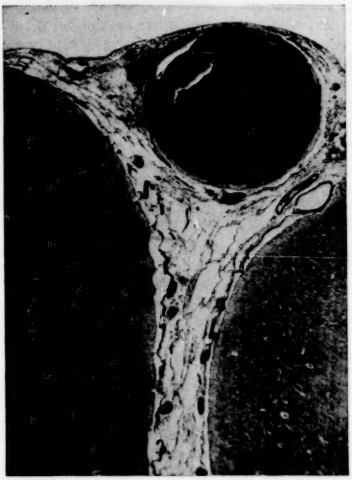

Fig. 2.—Cross section of cerebral vein showing recent thrombus.

hemorrhages of the coronary artery with canalization have been shown by Wartman [1] to be associated with arteriosclerosis. The recent mural thrombus of the right common iliac artery was not organized, and the underlying wall was slightly infiltrated with leukocytes. These changes are related to arteriosclerosis and are not considered to be due to thromboangiitis obliterans. Although autopsy examination revealed no arterial changes consistent with thromboangiitis obliterans, the clinical diagnosis was suggested by the occasional pain in the calves on exertion, the dusky red discoloration of the dependent feet, the blanching of the feet on elevation, and the absence of a palpable dorsalis pedis pulse of both feet.

COMMENT

In 1866 Paget [2] clearly described the clinical course in two cases of recurrent thrombophlebitis of the extremities of unknown cause. Since that time over 130 case reports of primary thrombophlebitis have appeared in English medical annals. The largest number of cases of this condition was described in 1936 by Barker.[3] He reported 79 cases of idiopathic thrombophlebitis of which 40 were recurrent. The latter occurred during middle life, affected males more frequently than females, and did not occur predominately in Jews. The superficial veins of the upper and lower extremities were chiefly affected, and short segments of these vessels became tender, red, firm, and sometimes nodular. The focal thromboses frequently subsided only to recur at another site on the same or opposite extremity, so that

1. Wartman, W. B.: Occlusion of the Coronary Arteries by Hemorrhage into Their Walls, Am. Heart J. **15**: 459 (April) 1938.
2. Paget, J.: On Gouty and Some Other Forms of Phlebitis, St. Barth. Hosp. Rep. **2**: 82, 1866.

a migratory character was noted and symmetrical involvement of the extremities was common. The episodes of thrombosis were accompanied by a low grade fever and slight polymorphonuclear leukocytosis. The attacks were recurrent and of varying duration, but the course was self-limited and recovery was ordinarily complete. Barker stated that clinically recognizable arterial lesions did not develop in most cases of idiopathic recurrent thrombophlebitis. The cause remains unknown, although Paget [2] attributed the condition to a defect of uric acid metabolism, Briggs [4] to phlebosclerosis, and Herrick [5] to an unidentified circulating toxin. In an epidemic of thrombophlebitis in East Africa, Manson-Bahr and Charters [6] emphasized that most of the patients had been given antisyphilitic injections of bismuth and arsenic, although they could not exclude a syringe-transmitted virus as the cause. This group of cases was unique in that most patients also had a stiff neck and relative lymphocytosis. In addition, these cases were sharply localized about two widely separated stations for the treatment of venereal disease. It has been thought that some cases of primary thrombophlebitis represent a venous component of thromboangiitis obliterans. Harkavy [7] found that, in a control group of 262 smokers, 43 were hypersensitive to intradermal injections of various tobacco extracts. However, in 78 patients with thromboangiitis obliterans, 76 were similarly hypersensitive whereas only two of five patients with thrombophlebitis migrans exhibited hypersensitive reactions. Also, Ackerman and Estes [8] in following 59 cases of thrombophlebitis migrans for five years reported that discontinuance of the use of togacco seemed to have little effect in preventing recurrences of thrombophlebitis. Further cases of primary thrombophlebitis of superficial veins were described by Zaus and others.[9]

In other cases there were clinical manifestations indicating involvement of deep as well as superficial veins. These cases were described by Collier and others.[10] The thrombosed deep veins as shown at autopsy included the hepatic, portal, gastric, splenic, gastroepiploic, superior mesenteric, and pulmonary veins as well as the inferior vena cava. In this type of case Barker [3] and Ackerman and Estes [8] emphasized the high frequency of pulmonary infarcts, and in the case of Birnberg and Hansen [11] the small intestine became gangrenous.

In several cases of primary thrombophlebitis there were recurrent clinical manifestations that indicated involvement of cerebral veins. These manifestations included convulsions, loss of consciousness, headache, coma, paresthesias, aphasia, and transient pareses. Most of the patients recovered so that anatomic examination of the affected vessels was not performed. However, in 1942 Bucy and Lesemann [12] described a 37-year-old man who had recurrent thromboses of the peripheral veins of four years' duration. He was then well until the age of 52, when periods of unconsciousness, intense frontal headaches, and muscle twitching of one arm developed. Craniotomy was performed, and distended, firm, thrombosed cerebral veins were observed. Tissue was not taken for histologic examination, and the condition gradually subsided. These authors were unable to find a previous description of the pathologic anatomy of a case of primary thrombophlebitis of cerebral veins. In 1947, Davis and Perret [13] described 11 patients who were thought to have cerebral thromboangiitis obliterans. However, in five of these, (cases 1, 2, 4, 6, and 9) no clinical manifestations of thromboangiitis obliterans of the peripheral vessels were described, and the diagnosis was based on the gross appearance of the cerebral vessels at the time of craniotomy. There was no microscopic examination of the cerebral vessels in these five cases and no statement as to whether the vessels were arteries or veins. It remains unproved that these cases were not examples of primary cerebral thrombophlebitis. Other cases of recurrent thrombophlebitis of peripheral vessels with clinical signs indicating cerebral involvement were reported by Barber and others.[14]

It was pointed out by Winiwarter [15] and later by Buerger [16] that thrombosis of superficial veins of the extremities occurs frequently in cases of thromboangiitis obliterans. This was called migratory phlebitis, and Buerger [16] emphasized that in most cases there were absent arterial pulsations or other signs to indicate that the patients had thromboangiitis obliterans. However, in the case of d'Abreu [17] migratory phlebitis preceded the development of thromboangiitis obliterans by 40

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11. Birnberg, V. J., and Hansen, A. E.: Thrombo-Phlebitis Migrans, J. Pediat. **21**: 775 (Dec.) 1942.

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14. Barber, H.: A Case of Thrombo-Phlebitis Migrans, Brit. M. J. **1**: 281, 1932. Ryle, J. A.: Thrombophlebitis Migrans, Lancet **219**: (Oct. 4) 1930. Flood, E. P.; Redish, M. H.; Bociek, S. T., and Shapiro, S.: Thrombophlebitis Migrans Disseminata: Report of a Case in Which Gangrene of a Breast Occurred, New York J. Med. **43**: 1121 (June 15) 1943. Campbell, M., and Morgan, O. G.: An Unusual Case of Multiple Thrombosis, Guy's Hosp. Rep. **80**: 34 (Jan.) 1930. Stern, N. S.: Thrombophlebitis Migrans, with a Report of 2 Fatal Cases with Autopsies: One Also Showing Primary Carcinoma of the Liver, South. M. J. **27**: 849 (Oct.) 1934. Kletz, N.: Thrombo-Phlebitis Migrans, Lancet **2**: 938 (Oct. 29) 1932. Gerber, I. E., and Mendlowitz, M.: Visceral Thrombophlebitis Migrans, Ann. Int. Med. **30**: 560 (March) 1949.

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years. Intervals of 20 and 11 years, respectively, were present between the onsets of the two conditions in the cases reported by Ficarra [18] and by Johnson.[19] Signs of cerebral disease during the attacks of phlebitis were not described in these three cases. Although this indicated that the two conditions might be related, Ackerman and Estes [5] stated that thromboangiitis obliterans developed in only 2 of 59 cases of thrombophlebitis migrans that were followed for over five years.

In a review of the clinical aspects of 500 cases of thromboangiitis obliterans, Hausner and Allen [20] found 11 cases in which there were signs indicating disease of the cerebral vessels. Similar cases were also described by Sunder-Plassmann [21] and by Barron and Linenthal.[22] Cases of cerebral thromboangiitis obliterans confirmed at autopsy were reported by Spatz and others.[23] The cerebral veins were specifically mentioned only in the case of Spatz. He stated that occasional vein walls were infiltrated with polymorphonuclear leukocytes and that some small veins contained scattered recent thrombi. However, thrombophlebitis of large cerebral veins or thrombosis of veins apart from inflamed arteries were not described.

SUMMARY

In some instances primary thrombophlebitis precedes or accompanies the development of thromboangiitis obliterans. It is not established that all or most cases of primary recurrent or migratory thrombophlebitis are associated with thromboangiitis obliterans. Primary thrombophlebitis of cerebral veins occurs in the absence of intracranial arterial disease. The clinical and pathologic features of such a case are described in a patient who had signs suggestive of thromboangiitis obliterans of the lower extremities. So far as can be determined, this constitutes the first record of the clinical course as well as the anatomic examination of such a case.

250 E. Superior St. (11).

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TREATMENT OF CHRONIC PULMONARY TUBERCULOSIS COMPLICATING SILICOSIS

INTERMITTENT POSITIVE PRESSURE BREATHING AND STREPTOMYCIN

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and
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Gaining ascendancy from the writings of Detweiler [1] (1878), rest in bed has become the traditional and essential treatment of pulmonary tuberculosis. However, since the advent of special drugs and procedures, there gradually has developed a regimen with definite indications and limitations for rest, both physical and physiological. It is recognized generally that the supplementary use of streptomycin is required for the acute exudative forms of tuberculosis with toxemia; but, in the chronic types with cavitation and persistent tubercle bacilli in the sputum, artificial pneumothorax, pneumoperitoneum, thoracoplasty or pulmonary resection may be indicated. There is increasing evidence that sustained rest in cases with emphysema is ineffectual, if not actually disturbing. Similarly, the employment of collapse therapy for atelectasis is harmful, owing to impaired drainage and aeration. Thus, closely associated in treatment are the aspects of a disease for which dynamic therapy as well as rest should be considered.

In an interesting discussion of rest as a therapeutic measure Dock [2] mentions that the pathology of tuberculosis is usually localized in the apex of the lungs. He suggests that the developments of tuberculosis bear some relationship to the level of the pulmonary arterial pressure and the associated factors of lymph formation, antibody distribution, and toxin elimination. It is noted in a further consideration that tuberculosis is rare in mitral stenosis [3] and that a high frequency of the disease occurs in cases of pulmonic stenosis.[4] The preventive mechanism in the former cases is attributed to the relatively high pulmonic arterial pressure (116 mm. Hg and usually over 40 mm.), while the important factor in pulmonic stenosis supposedly is the bloodless condition of the apex related to lower pulmonic pressure, even during the peak of physical activity.

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Studies in animals show a development of apical tuberculosis similar to that in man. Medlar and Sasano [5] observed that the disease in rabbits and cattle occurs typically in the parts of the lung nearest the diaphragm, close to the spine. Surprisingly, the process will shift from the juxtadiaphragmatic region to the apexes after the animals are maintained in the erect position for periods of 11 hours daily. This transposition is ascribed by Dock to the relatively inadequate blood flow farthest away from the heart in the gravitational field.[2]

In referring to the hypothesis that increased pulmonary arterial pressure may participate in the control of tuberculosis, recent observations suggest that significant variations of pressure should not be anticipated. It is observed, for instance, in normal subjects during exercise that there is no increase of the pulmonary artery pressure and, contrarily, the pulmonary vascular resistance is decreased.[6] Contrasting are the observations in chronic pulmonary disease indicating that the resting pulmonary arterial pressure may be normal, and in certain instances the elevated pressures at rest may be further increased during exercise.[6] The observation that acute hypoxia tends to elevate pulmonary arterial pressure [7] adds complexity to the problem. Thus, it would appear that recumbency in itself is not a specific mechanism for elevating pulmonic arterial pressure. This concept is elaborated with the observation that the pulmonic blood pressure in valvular heart disease is not necessarily limited to the apexes; actually the arterial pressure changes are essentially the same throughout the lung fields.

The quiescence and abeyance of tuberculosis are sometimes attributed to pulmonary fibrosis. Accordingly, the fibrotic process has been regarded as an effective development in the mechanism of healing. While there has been recognition of the potential influence of fibrosis, there is the curious paradox of impaired pulmonary function attributable to destroyed alveoli, bronchioli, and blood vessels, penalizing the useful factors of fibrosis.

With special reference to the mechanism of fibrosis, certain aspects have appeared in recent studies of tuberculosis complicating silicosis: It was disclosed that 97 cases in a group of 750 coal miners admitted to the hospital without selection were affected with tuberculosis.[8] An interesting feature was the relative high occurrence during the fourth and fifth decades of life, as compared with the higher frequency in the second and third decades of city dwellers unaffected with silicosis. Thus, there is the speculation that silica or the fibrosis is a predisposing cause of tuberculosis, with a supplementary influence of retardation as induced by the fibrous tissue. An additional aspect of the study relating to the course following the onset of manifest tuberculosis indicated that longevity was two to three years among those treated at home. In contrast was the experience at the White Haven Sanatorium, where certain coal miners undergoing systematic care lived 5 to 10 years or more, suggesting that medical care in itself was more valuable than the factor of fibrosis. Indeed, the issues of fibrosis appear complex and variable.

In recent years, the role of segmental and lobular physiology in the development and perpetuation of chronic pulmonary diseases has aroused considerable interest. The basic aspects relate to ventilation alveolar tension, and the unique mechanism of capillary blood drift and intra-alveolar air drift, as discussed by Churchill.[9] It is mentioned that a minor pulmonary embolism will disclose a collateral drift in the pulmonary capillary network of sufficient magnitude to maintain a slowly moving circulation, despite occlusion of the sizeable terminals of the pulmonary artery. This is illustrated in cases with increased back pressure in the pulmonary veins or abnormal slowing of the capillary stream by reduced respiratory excursion when a bland infarct may be converted into a hemorrhagic infarct. Churchill [9] suggests that this capillary blood drift crosses the segmental boundaries of the lung. With the collateral air drift there also are the features of a compensatory mechanism or an emergency device of respiration. The sequence of events relates to the trapping of air in the alveoli by obstruction to its outflow and the effects of cough, characteristic of pneumonia or paroxysmal asthma, as follows: (1) inspiratory widening of the terminal bronchioles; (2) early in expiration the quick closure of the laryngeal sphincter with elevation of the endobronchial air tension by the muscular effort of a cough or grunt; (3) trapping of air in lobules under increased tension; and (4) slow reduction in the tension by collateral air drift through the pores so that in the next cough the lobule receives a blast of fresh air with renewed oxygen supply. The importance of the collateral air drift of the lungs was emphasized in World War II, when aspiration of blood and secretions from the pleura and air passages, and the employment of intercostal nerve block replaced the earlier practice of using morphine and tight strapping of the chest, resulting in a remarkable reduction of postoperative edema. While the blood drift may be less important than air drift as a compensatory mechanism of respiration, since the blood has already passed through functioning alveoli with resultant oxygenation, there is the influence of blood in maintaining the integrity of capillary walls.

The normal mechanism of chronic pulmonary conditions relates to the preservation of the whole dynamic action of the respiratory system with its adequate ventilation and active capillary circulation. This involves the elaborate neuromuscular structure surrounding the air passages and the constant and vigorous activity of the bronchus. Of special interest is the inspiratory dilatation and lengthening of the bronchi, and constriction with shortening during the expiratory phase.[10] It is apparent that integration of pulmonary ventilation and alveolar

5. Medlar, E. M., and Sasano, K. T.: A Study of Pathology of Experimental Tuberculosis, Am. Rev. Tuberc. **34**: 456 (Oct.) 1936.
6. Riley, R. L., and others: Studies of the Pulmonary Circulation at Rest and During Exercise in Normal Individuals and in Patients with Chronic Pulmonary Disease, Am. J. Physiol. **152**: 372, 1948.
7. Motley, H. L.; Cournand, A.; Werko, L., and Dresdale, D.: The Influence of Short Periods of Induced Acute Anoxia upon Pulmonary Artery Pressures in Man, Am. J. Physiol. **150**: 315, 1947.
8. Theodos, P. A., and Gordon, B.: Tuberculosis in Anthracosilicosis, Nat. Tuberc. A. Tr. 47th Annual Meeting, **47**: 258, 1951.
9. Churchill, E. D.: The Segmental and Lobular Physiology and Pathology of the Lung, J. Thoracic Surg. **18**: 279, 1949.
10. Macklin, C. C.: The Musculature of the Bronchi and Lungs, Physiol. Rev. **9**: 1, 1929.

air tension, with preservation of the bronchiole and respiratory bronchiole at the site of the sphincters surrounding the necks of the air sacs, is an important prerequisite for normal function.

With reference to the minute processes of the respiratory system, the secreting membrane of the segmental bronchus introduces a peculiar factor of obstruction to the air passages that may not occur at the bronchiolar level. As a consequence, blockage of the segmental bronchus and retrograde filling or drowning of the bronchioles and air sacs will result.[11] However, as Churchill [9] observed in two children with the so-called Kartagener syndrome, the developments were relatively benign in the absence of infection. This absence of pus was attributed by him to the timely use of antibiotics and reexpansion of the pulmonary segments. In another case of Kartagener syndrome, bronchiectasis followed an attack of acute bronchitis.[9] From these interesting considerations, it appears that the combined influences of impaired ventilation elaborated in the disturbances of abnormal air drift and blood drift pose important problems in the treatment of most cases of chronic pulmonary disease, fibroid tuberculosis with emphysema being no exception.

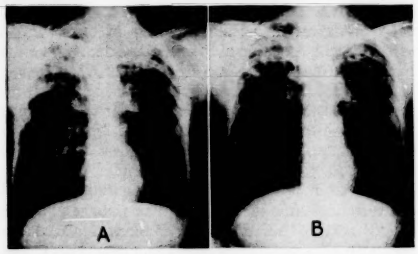

Fig. 1.—H. B., male, 52, with the diagnosis of fibroid type tuberculosis (apical) of both lungs with tubercle bacilli in the sputum and the manifestations of marked pulmonary emphysema. *A* (Nov. 29, 1949), obtained before treatment with intermittent positive pressure breathing. *B* (Oct. 12, 1950), taken after six months' treatment; symptomatic improvement with reduction in the areas of increased density were attributed to improved bronchiolar drainage and alveolar aeration.

In the physiological disturbances of emphysema per se, there is a faulty distribution of air in the lungs. This impairment of function is attributed to mixing and dilution difficulties with unequal alveolar aeration and perfusion caused by the loss of pulmonary elasticity and obstructive changes in the bronchioles, accentuated by inspissated mucus, fibrous contraction, or bronchospasm. Inadequate distribution of inspired air lowers the alveolar oxygen partial pressure (pO_2) and the percentage saturation of arterial blood oxygen due to the elevated mean pO_2 gradient between the alveoli and the arterial blood. In some cases the increased mean gradient of pressure for oxygen between the alveoli and arterial blood approaches 50 mm. Hg (normal, 5 mm. Hg), and the average resting arterial oxygen saturation is moderately reduced but poorly correlated with pulmonary function impairment.[11] It is interesting that the arterial oxygen saturation values obtained during mild exercise may reveal significant differences with respect to disability and the degree of emphysema, as compared with the resting level.

Fatigue, an important influence in disability, reflects the results of physical effort, lack of proper rest, and disturbed pulmonary function. This is notable in silicotic coal miners plagued with paroxysmal racking cough and dyspnea. In the progressive cases, rest in bed is possible only while the patient is lying with the back supported on two or more pillows; with advanced disease the patient can obtain rest only in a reclining type of chair or in a straight chair, while leaning forward with the arms hanging down or supported on a window sill or table. Other factors participating in the phenomenon of fatigue are restricted exercise and the occurrence of acute chest colds involving the bronchioles.[12] There are both the innate and direct disturbances of the structural disease with the concomitant factors of a vicious circle. For example, with enforced rest there is impaired pulmonary ventilation, and with insufficient rest the ramifications of lowered resistance are brought into play.

The treatment of uncomplicated silicosis relates to (1) symptomatic relief for dyspnea and choking cough; (2) measures that favor the drainage of "free silica" and abnormal secretions of the bronchioles; and (3) improvement of respiratory function with dynamic therapy.[13] It has appeared that therapeutic rest in bed is contraindicated, since the important requirements are for the acceleration of bronchial drainage and restored alveolar aeration. The use of respiratory exercise as obtained with intermittent positive pressure breathing treatments provides a midway course in favoring pulmonary function without the handicaps of overexertion.[13] A pertinent question has occurred with the discovery of tuberculosis during the course of the treatments (four cases): Is intermittent positive pressure breathing therapy indicated or contraindicated in tuberculosis? Indeed, there has been a dilemma when symptomatic relief from the silicosis occurred in the shadow of the possible aggravation of tuberculosis. While recalling the unsatisfactory results from the accepted treatment of tuberculosis in this type of patient, our interest turned guardedly to the use of intermittent positive pressure breathing.

The present observations are based on the study of 18 cases of tuberculosis with extensive fibrosis, emphysema, tubercle bacilli in the sputum, and the symptoms of dyspnea, weakness, racking or choking cough, and difficult expectoration. It is emphasized that these patients were classified as "old chronics" with limited manifestations of active tuberculosis, the chief disturbance being physiological as related to the associated pulmonary conditions. Actually, the diagnosis was established only with the discovery of tubercle bacilli in the sputum and the presence in the x-rays of localized apical densities with or without cavitation and deviated trachea. A series

11. Motley, H. L.; Gordon, B.; Lang, L. P., and Theodos, P. A.: Impairment of Pulmonary Function in Anthracosilicosis, Arch. Indust. Hyg. **1**: 133, 1950.
12. Gordon, B., and others: Considerations of the Clinical and Physiologic Factors in the Treatment of Chronic Pulmonary Conditions, Dis. Chest **19**: 271, 1951.
13. Gordon and others.[12] Motley, H. L.; Lang, L. P., and Gordon, B.: Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Pulmonary Disease, Am. J. Med. **5**: 853, 1948.

of six additional cases of arrested or suspected tuberculosis, nonsilicotic in type, are included, since the manifestations and basic problems simulated silicosis with complicating tuberculosis. It was observed that previous treatment with enforced rest in the recumbent position had been generally ineffectual because of the respiratory symptoms, and artificial pneumothorax and thoracoplasty were contraindicated. Continuous immobilization of the lungs by residence in an equalizing chamber,[14] a method advocated for treatment in certain cases of tuberculosis with cavitation and acute disease, was deferred (Fig. 1), because it appeared that this form of pulmonary restriction favored the retention of secretions and consequent dyspnea. With reference to drug administration, it had been noted repeatedly that narcotic preparations reduced cough but coincidentally lessened expectoration, accentuating the difficulties of reduced pulmonary aeration. The action of bronchodilator drugs given by aerosol was disappointing.

In the physical examinations, the occurrence of dyspnea, cough, expectoration, elevated temperature, accelerated pulse rate, and rales, and the presence of tubercle bacilli in the sputum were tabulated before, and after the course of treatments for indications of improvement or aggravation. Roentgenograms of the chest also were obtained before and during the treatments and one, two, three, or six months later.

The regimen of intermittent positive pressure breathing treatments,[15] consisting of 100% oxygen and racemic epinephrine solution (vaponefrin,* 8 drops diluted in an equal amount of isotonic sodium chloride solution) was employed for periods of 5 to 15 minutes, once or twice daily, with discontinuance for three or four days when there was relative freedom from disturbing pulmonary symptoms.[16] The maximum period of treatment was three months, except in two patients, who had received the treatments, with interruptions, for more than one year. Of the entire series, nine were hospitalized continuously; others were treated alternately in the hospital and at home. Streptomycin, 1 gm. daily, was given parenterally (simultaneously) in five patients with a high number of tubercle bacilli in the sputum. All patients followed their customary habits of sleeping and resting, which were variable, owing to the dyspnea.

The following data were noted: A constant feature was the reduction of dyspnea and choking cough with increased expectoration, initially, followed by reduction of the sputum, the improvement being characteristic in coal miners with uncomplicated silicosis. With lessened dyspnea there was the expressed desire to rest in bed, often in the recumbent position. Improved appetite, a sense of well-being, and a gain of 2 to 4 lb. (1 to 2 kg.) occurred in nine cases. The increase of tubercle bacilli, followed successively by a decrease, was an interesting feature in three cases. In one instance the sputum displayed transiently a variety of colors and tenaciousness. The physical signs, including alterations in the percussion note, rales, and exaggerated breath sounds, were not permanently influenced. It was striking, however, that after each treatment there usually was a transient reduction of musical rales, sometimes associated with louder breath sounds and freer movements of the chest. These alterations, found also in uncomplicated silicosis treated with intermittent positive pressure breathing, were attributed chiefly to increased bronchiolar drainage and alveolar aeration, rather than to specific effects on structural disease. In the x-rays there were no appreciable changes in the type or distribution of the shadows, except in two cases in which there were large radiolucent bodies in the areas formerly occupied by dense shadows and two cases with suggestive extension of the tuberculosis; in two cases there was striking regression (Fig. 2). It is interesting that the appearance of the radiolucent structures was coincidental with marked expectoration and the increased number of tubercle bacilli in the sputum. One patient died in the third week of treatment, during an acute episode of intercurrent infection with a possible extension of the tuberculosis; two died approximately six months after the treatments were terminated. Therapy was discontinued in two instances because of persistent elevation of temperature and weakness, with

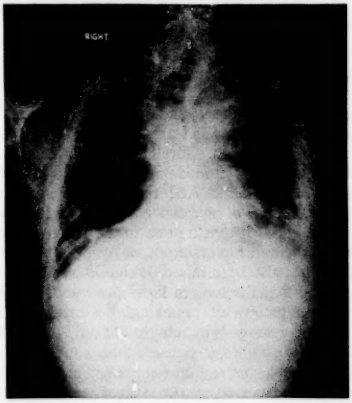

Fig. 2.—Male, age 31, with fibroid pulmonary tuberculosis (apical and basal) and marked emphysema. Marked dyspnea with difficult expectoration followed a period of prolonged rest in bed and residence in an immobilizing chamber; intermittent positive pressure breathing treatments reduced the dyspnea and facilitated expectoration.

a suggestive spread of the tuberculosis. It is of interest that seven patients requested a resumption of the treatments, previously discontinued for clinical evaluation. These requests were based on the increasing dyspnea and the inability to expectorate effectively.

The present use of intermittent positive pressure breathing treatments in tuberculosis was undertaken primarily as a means to determine the effects of bronchiolar and alveolar dilatation and improved pulmonary drainage on the immediate and subsequent course of the disease, with special reference to symptomatic improvement and the ability of the patient to rest more adequately in

14. Barach, A. L.: Continuous Arrest of Lung Movement; the Treatment of Pulmonary Tuberculosis in an Equalizing Alternating Pressure Chamber, Am. Rev. Tuberc. 43: 56, 1941.

15. The apparatus is manufactured by V. Ray Bennett, 8154 Beverly Blvd., Los Angeles, and The Mines Safety Appliances Company, Pittsburgh.

16. The usual periods of treatment with intermittent positive breathing are 20 minutes, two or three times daily for several weeks or months; the reduced periods in the present tuberculous cases were preferred in order to avoid possible fatigue.

the recumbent position. The rationale was based chiefly on the concept that maximum rest ordinarily indicated for tuberculosis was impossible, because of dyspnea, choking cough, difficult expectoration, and their fatiguing and traumatizing influences. It had been recognized that abnormal bronchiolar and alveolar secretions interfered with the mechanism of alveolar aeration and perfusion, favoring the development of new disease and the concomitant functional disturbances. In the over-all consideration, the tuberculous infection per se appeared less disturbing than the vagaries of physiologic dysfunction. The findings emphasize that symptomatic relief from dyspnea and difficult expectoration occurred with about the same constancy as would be expected in uncomplicated silicosis.

There has been speculation as to the possibility that increased activity of the tubercle bacilli occurs under the influences of 100% oxygenation, as introduced under intermittent positive pressure breathing. The question is pertinent, since the report of Rich and Follis [17] indicated that the growth of tubercle bacilli experimentally may be influenced by increased oxygen tension. There are no data in the present study suggesting that increased oxygenation in itself caused untoward effects. Indeed, it would appear that the immediate action of oxygen bacteriologically, if any, was transient, since the treatments were of short duration. More important, perhaps, is the concept that, with improved aeration of the alveoli, the advantages of symptomatic relief would outstrip the theoretical hazard of new activity of tuberculosis organisms. The question that trauma to the lungs may result from the increased pressure of oxygen with forced inspiration has also been raised. It should be noted in this connection that the oxygen flows according to the patient's own pattern of breathing, the maximum peak inspiratory pressure being equivalent only to 20 cm. of water, a distinctly lower pressure than would occur even in minor cough (maximum pulmonary pressure during cough varies from 40 to 100 cm. of water, or more), and the pressure becomes atmospheric during expiration. As the lungs are filled with oxygen under the mechanism of intermittent positive pressure breathing, the rate of flow is approximately one-half the flow rate during the initial phase of expiration. Actually, the flow of expiration exceeds the force of inspiration, owing to the rapid drop of pressure during expiration. With this mechanism, the passage of mucus down the bronchial system during inspiration is minimal, as compared with the flow rate that favors an upward movement of mucus. In a sense, the phenomenon of expiration simulates the mechanism of cough in a very reduced manner. With reference to the efficiency of cough, it should be emphasized that the mechanism operates effectively only when air is present in the alveoli. This is elucidated in acute atelectasis, when the pathological and physiological conditions deprive air from the affected region and prohibit the expulsion of contents. In such conditions treated with the combination of helium, 30% or 40%, and oxygen, 60% or 70%, introduced under intermittent positive pressure breathing therapy for periods of 20 minutes every four hours, remarkable expansion of the lung is sometimes noted.

Admittedly, the paradox of employing intermittent positive pressure in silicosis with complicating tuberculosis is not easily composed, in light of the value and indications for rest as a therapeutic measure. As mentioned previously, the indications are weighed in the balance between respiratory quietude and increased alveolar aeration that may be harmful or valuable, respectively. It should be re-emphasized that the accomplishments of intermittent positive pressure breathing in chronic pulmonary tuberculosis are not curative. The procedure is used primarily in the channel of symptomatic relief in order to obtain ultimately the resultant benefits of adequate pulmonary function, as indicated in pulmonary emphysema and inoperable bronchiectasis.[12]

SUMMARY AND CONCLUSIONS

1. The present study, dealing with chronic pulmonary tuberculosis associated with anthracosilicosis, indicates that the physiological disturbances of emphysema and fibrosis are basic causes of dyspnea, racking or hacking cough, and difficult expectoration.

2. Rest in bed with so-called collapse therapy, the accepted treatment in pulmonary tuberculosis, is not always applicable, since respiratory quietude sometimes accentuates the disturbances of emphysema and fibrosis of the lungs.

3. Intermittent positive pressure breathing treatments with aerosols of bronchodilator drugs have been employed guardedly in a selected group of chronic pulmonary tuberculosis with emphysema and fibrosis; streptomycin was administered as supplementary treatment in cases with suspected acute exacerbations of the disease.

4. The relief of manifestations, as noted in the majority of the cases, was attributed to improved pulmonary drainage and alveolar aeration.

5. The symptoms and function disturbances of emphysema and fibrosis of the lungs associated with pulmonary tuberculosis pose the fundamental need for physiological adjustment, without which the normal processes of healing may be retarded.

6. The aspects relating to the development and dissemination of pulmonary tuberculosis are reviewed.

17. Rich, A. R., and Follis, R. H., Jr.: Effect of Low Oxygen Tension upon the Development of Experimental Tuberculosis, Bull. Johns Hopkins Hosp. **71**: 345, 1942; abstracted, Tr. A. Am. Physicians **57**: 271, 1942.

Peptic Ulcer in Children.—It is apparent that peptic ulcer does occur frequently in children and that its likelihood must always be considered whenever persistent gastrointestinal disturbance occurs. The peptic ulcers of childhood are usually acute in type during infancy. The onset of symptoms is often precipitous and without recognizable premonitory symptoms or signs. The majority of the lesions in this age group either bleed profusely or perforate. As the age of the child increases, the type of ulcer increases in chronicity. The incidence of bleeding and perforation diminishes and the likelihood of pyloric stenosis and scarring of the duodenum becomes greater. The probability of persistent abdominal pain, frequently of the adult type, also increases. The prevalence of peptic ulcer in children is somewhat greater in the male than in the female (approximately by a 3 to 2 ratio in all age groups). Also, duodenal lesions occur more frequently than gastric.—Russell H. Morgan, M.D., Peptic Ulcer in Children, *The American Journal of the Medical Sciences*, November, 1951.

MEDICAL IDENTIFICATION IN THE "NORONIC" DISASTER

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and
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The identification of large numbers of mutilated bodies may be among the many difficult problems to be faced in major disasters resulting from fire or explosion. Such was certainly the case when the steamship "Noronic" was gutted, while tied up at the pier in Toronto, Canada, on Sept. 17, 1949. The deaths of 119 persons were directly attributable to the disaster, and the bodies of 107 were burned beyond possible recognition. The task was undertaken by a Medical Identification Committee, composed of pathologists, radiologists, and dentists.[1] This group succeeded in identifying 116 of the 119, and the results have never been equalled. In these uneasy times, when extensive preparations against disaster are being made, the experiences and achievements of such a medical study deserve a place in the records.

The identification of burned bodies is not a new problem, and it has been met on a large scale in several recent fire disasters. Four hundred ninety-one persons lost their lives in the fire at the Cocoanut Grove in Boston in 1942.[2] Plans laid during World War II in the Disaster Preparedness Program of the Boston Area encompassed such an eventuality, and almost all the bodies were identified within a few days. The majority of the deaths resulted from suffocation, and most of these bodies were not badly disfigured. Jewelery, clothing, wallets, and keys on the bodies, as well as facial features, were preserved and were easily recognized by relatives and friends. The attending physicians were fully occupied with the care of many persons with serious burns and, apparently, played no part in the identification of the dead. In the Texas City explosion [3] in 1947, between 500 and 600 were killed. All but 61 mutilated bodies were identified by the Texas State Safety Council. The medical services were taxed to the limit in attending more than 3,000 casualties and were not involved in the identification plan. Autopsy was performed on only a few bodies. In both the Hartford circus tent fire and the more recent explosion at South Amboy, N. J., the identification work was left to the police. Indeed, identification in general has become a special branch of scientific police procedure. Fingerprinting, which has proved to be the most accurate method, is the basic technique in identification, but several others are employed. Dental examination may be used when the body is decomposed or mutilated, but very seldom is anatomic evidence necessary.

In the "Noronic" disaster the devastation wrought to such a large number of bodies put the possibility of identifying many of the victims beyond the limitations of the usual techniques of identification. One hundred and eleven charred bodies were recovered from the ashes and twisted wreckage of the ship, and all but four of these were burned beyond recognition. Five other persons were drowned in the harbor beside the ship, and one woman was dead on arrival at the hospital from injuries received while escaping the fire. Although a number of survivors were treated for minor burns in the emergency wards of the hospitals, relatively few persons with serious burns were found, and only two women died in the hospital some weeks after the fire. The bright red blood of the body in most of the burn victims suggested that carbon monoxide poisoning caused death, rather than the burns, but it was thought that little could be gained in attempting to prove this point under the circumstances of this catastrophe. The major problem in the "Noronic" disaster was identification of the dead.

A general résumé of the extent of the burns gives some understanding of the difficulty of the situation. In 49 bodies every square inch of skin and subcutaneous tissue was burned away, and all the underlying muscles were charred. In only 20 bodies was there sufficient skin remaining on the fingers to enable the taking of fingerprints. In 86 bodies the calvarium was burned open, in 73 both sides of the thoracic cage were destroyed, and in 85 the abdominal wall was demolished. In only 16 cases did all four extremities remain intact, although charred, and in 22 cases all four extremities were absent. Those limbs, or parts of limbs that remained, often consisted only of cracked fragments of bone held together by blackened muscle. This limited the possibility of using such calculations as Pearson's formulas for the estimation of height. The bodies were made rigid by the burns, and the joints were frequently burned open.

Besides the damage to the bodies, there were other difficulties to be met. What property remained on the bodies was badly destroyed. There was nothing to indicate the site on the ship where each body had been found. When it came to determining who was lost in the fire, the disaster relief teams found themselves in a predicament. There was, at first, no passenger list for the ship, and this, combined with the failure of some survivors to report their escape, increased the lists of the missing. Then, none of the casualties were known to local residents, because all of the ship's passengers were tourists, the majority of whom came from Cleveland, Detroit, and surrounding communities. The relatives and friends of the missing, were, also, in strange surroundings when they came to Toronto, and this, together with their anxieties, added further to the confusion.

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This project was conducted under the direction of the Honorable Dana M. Porter, Attorney-General of the Province of Ontario, and Hiram E. McCallum, Mayor of the City of Toronto. The City of Toronto and the Province of Ontario shared in the entire cost of the investigation.

1. The members of the Medical Identification Committee for the "Noronic" disaster were Dr. W. L. Robinson (Chairman); Drs. A. C. Singleton, E. A. Grant, T. C. Brown, R. J. Delaney, W. Anderson, J. Simpson, F. Bryans, G. Cates, H. Cleland, and D. Wilson.

2. Aub, J. C.: Management of the Cocoanut Grove Burns at the Massachusetts General Hospital, Philadelphia, J. B. Lippincott Co., 1943.

3. Blocker, V., and Blocker, T. G.: The Texas City Disaster; Survey of 3,000 Casualties, Am. J. Surg. **78**: 756, 1949. Identification in Disaster: Texas Department of Public Service, 1948.

It was necessary, for several reasons, to identify those who died in the fire, but the first consideration was the personal feelings of the relatives and friends, who could never rest until the deaths of their lost ones could be established beyond doubt. On the other hand, the fire created a wide range of mundane problems, of which a swift resolution was of equal import to those grieving persons. There were wills to be probated and estates to be settled. Insurance payments and claims awaited the issuance of death certificates, and premium payments had to be continued until this was forthcoming. Business associations, partnerships, and other arrangements were dislocated. There was the question of remarriage of survivors. In addition, it was important to forestall fraudulent attempts to collect insurance and false claims of death, and to guard against the desire of some persons to disappear. Therefore, there was every justification for embarking on an attempt to identify the victims.

TABLE 1.—*Lesion or Condition Discovered at Autopsy and Used in Identification*

Organ		Lesion or Condition	Case Incidence
Appendix		Perforation (old)	1
Bones	Spine	Scoliosis	1
		Kyphosis	2
		Osteoarthritis	7
	Knees	Osteoarthritis	1
	Os calcis	Osteoarthritis	1
	Mandible	Atrophy	1
Kidney		Polycystic (bilateral)	1
		Pyelonephritis, chronic	1
		Hydronephrosis	1
Lung		Calcareous degeneration (apical)	1
		Collapse (pneumothorax)	1
		Bronchiectasis	1
		Tuberculosis (treated)	2
Ovary		Corpus luteum	1
		Cyst, follicular	1
		Graafian follicles	1
		Atrophy	1
Pericardium		Pericarditis (fibrous)	1
Peritoneum		Adhesions	1
		Hernia	3
Pleura		(Adhesions) Fibrous pleurisy	2
Skin		Pilonidal sinus	1
Uterus	Cervix	Nulliparous	1
	Body	Premenstrual endometrium	1
		Menstruation	2
		Atrophy	1
		Prolapse	1
		Leiomyoma	2

Against the mutilation of the bodies in the "Noronic" disaster all the recognized techniques of identification had to be employed. They were modified to suit the special circumstances, and new ones were developed. A significant advantage was gained when it was proved that the number of persons missing in the fire tallied exactly with the number of bodies in the mortuary. The Red Cross had been able to compile an accurate passenger list by tracing every survivor and eliminating all but the "Noronic" victims from among the general missing persons' lists. Consequently, the proposition developed into a comparison of bodies with missing persons, and the study divided itself into two parallel investigations—the examination of the bodies, and the search for information on the missing persons. Both phases of the investigation were conducted simultaneously and by the same personnel. The former will be considered first.

The examination of the bodies included an autopsy, a dental study, x-ray examinations, fingerprinting, and a thorough description of all property and valuables on the body. Where indicated, special anatomic and chemical studies were done. The pathologists, radiologists, and dentists were aided, when necessary, by such specialists as were needed from the staffs of the University of Toronto, the Toronto General Hospital, and the City Department of Health. Working in conjunction with these men were the Toronto police force, who attended to the identification and protection of property on the bodies, the Federal Bureau of Investigation, who did the fingerprint studies, and the Canadian and American Red Cross, who conducted the social service work and maintained teletype communication between Toronto and the cities and towns all across the United States that could supply information about the victims. All these examinations took place at about the same time, and each will be dealt with in turn.

The autopsies were begun the day after the fire, and only an initial general examination of each body was completed on that day. As the bony structures could not be disturbed until the roentgenograms were made, particular attention was paid at this stage to listing the damage from burns on the bodies. When the roentgenograms were completed the autopsies were carried further, and special care was taken to preserve the tissue, so that none of the evidence would be destroyed. The viscera were, insofar as was practical, sectioned in situ. The signs of old injuries and operations were sought especially, as were developmental abnormalities. The internal organs were found badly charred whenever the abdominal and thoracic walls had been destroyed. The liver, lungs, and spleen were usually shrunken and dried, and the heart was hardened. The brain was almost always a putty-like mass, whether or not the calvarium was intact. The kidneys and pelvic viscera were usually preserved, as were the intestines, except for exposed loops, which were burned away. The adrenals and pancreas were always intact. Where indicated, sections for microscopic study were taken. Decomposition of the bodies was never a serious problem, because they were charred and because they were stored in an unheated building. The soft tissue that remained was protected by keeping the bodies in metal sealers with carbon dioxide ice and formaldehyde ("formalin")-soaked rags.

Despite the destruction of the bodies, the autopsies revealed a wide variety of lesions. Among those that were of value in identification were osteoarthritis of the spine in seven instances, inguinal hernia in three, and in two cases each kyphosis, pulmonary tuberculosis, pleural effusion, leiomyoma of the uterus, and menstruating endometrium. Table 1 lists these, together with those that played a part in single cases. Congenital abnormalities of the skeleton were found in two cases and, in each, formed part of the evidence. These deformities were spina bifida and an android pelvis. Signs of old injuries were found in only a few cases, but, again, all were useful in identification. There were two cases in which the eyes had been destroyed. There was one case in which the scar of an old penetrating injury of the anterior abdominal wall was found. In only two cases were old fractures discovered, one in the left metatarsus and the other in the left ankle. A wedge-shaped deformity of the second and third lumbar vertebral bodies was also included in this group. The manifestations of previous surgical procedures were a common finding and entered

oftenest into the identifications. In 18 bodies an appendectomy had been done, and in 9 of these this evidence was a necessary item in their recognition. Similarly, four bodies were recognized partially through an old cholecystectomy; three others showed this operation, but this information was not used. Table 2 lists the congenital abnormalities, old operations, and previous injuries, together with their incidence as a factor in identification. Many other lesions were found but are not listed here, because they were not made use of in this project and, still more, were never included in the autopsy records because the exigencies of the disaster prevented the examination of a body beyond what was necessary to establish its identity.

The dentists examined 87 of the bodies. Twelve bodies had been identified before dental studies were made, and in 14 more the jaws and mouth had been destroyed by fire. When necessary, dentitions were reexamined, an x-ray examination made, and the dentures submitted to specialists from manufacturing laboratories. The details of the dental investigation are to be published by Dr. E. A. Grant.[4] As with other phases of the plan, destruction of the jaws and teeth obscured the full details of the dentitions, and several types of dentures were hopelessly distorted or even disintegrated by the heat.

The fingerprint examinations were also difficult to make, and, in the bodies in which sufficient skin did remain, the ordinary methods of obtaining the finger ridge patterns could not be used. The fingers were therefore sent to the F. B. I. in Washington, where the skin was cut from their palmar surfaces. After softening, the sheets of skin were pressed between glass plates, so that the patterns could be photographed. The homes of the missing persons were searched for their fingerprints, and the patterns sent for comparison. In no cases, however, did this bring to light any valuable evidence.

The postmortem of the bodies by x-ray was an entirely new project. In 1926 Culbert and Law [5] reported the identification of a body by roentgenographic means, 216 days after the disappearance of the person, and, in 1944, Dutra [6] described the identification of a body burned beyond recognition in an automobile, but, apart, from these two cases, such a study had not been reported. Seventy-nine bodies were examined in the "Noronic" investigation. Insofar as possible the views made duplicated those used in clinical roentgenology, but the brittle state of the bodies, and the deformity and stiffening produced by the burns, made this difficult, and the films were clouded by metallic and amorphous foreign bodies, which obscured the bony outlines to some extent. The serous surfaces were flecked by sand, ashes, and embalmers' hardening compound, and melted and chipped paint was embedded in soft tissue. When the bodies had been washed out, the bony structure was cleared considerably. In all, 1,020 films were used, amounting to an average of 13 per person.

A thorough search of the ship's wreckage brought forth much evidence of adjuvant value to the investigators. Correlation of the sites where fragmentary human remains and personal property were found, with the ship's deck plan and the steward's lists of cabin allocations, gave corroberative evidence in several cases and sometimes provided the key to the solution of an identification.

From the reports of all the different examinations of each body a dossier was made, and care was taken to add to it additional evidence, correspondence, or notes pertaining to that body. To use in identification such a mass of information on more than 100 bodies the data had to be classified. This was begun after the initial examinations of the bodies had been completed and was amplified as more information was obtained. The bodies were categorized in accord with their features in common, and old operations, height, weight, age, dental characteristics, and property were prominent groupings. This system facilitated the search for bodies that might answer the description of some missing person.

The analagous side of the identification was the collection of information about the missing persons. This required a prolonged investigation, which was, as has been

TABLE 2.—*Identification Value of Abnormalities Found in Victims*

	Total Cases	Abnormality Valuable in Identification, No. of Cases
Congenital Abnormalities		
Spina bifida	1	1
Android pelvis	1	1
Operations		
Appendectomy	18	9
Circumcision	6	1
Cholecystectomy	7	4
Bronchogram	1	1
Enucleation	2	2
Herniorrhaphy	1	1
Hysterectomy		
Total	4	4
Subtotal	1	1
Ligation of fallopian tubes	1	1
Mastoidectomy	1	1
Pneumothorax	1	1
Oophorectomy	3	2
Sinusectomy (pilonidal)	1	1
Thyroidectomy	2	1
Previous Injuries		
Fractures		
1st metatarsal	1	1
Left ankle	1	1
Laceration of the anterior abdominal wall (R. L. Q.) (motorcycle accident)	1	1
Perforation of orbit oculi	2	2
Deformity (wedge shape) L_2 and L_3	1	1

mentioned previously, parallel to the autopsies. At the outset, any person seeking someone lost in the fire was interviewed by a social service worker who recorded a general description of the missing person, his address and those of his relatives and business associates, and such general information as might be useful. The next step was to examine the property recovered from the ship and the valuables held by the police. When this had been done, the relative was brought, with the form filled out by the social worker, to the pathologists and the dentists, who used this form as the basis for opening their files on a particular missing person. Relatives were frequently asked about serious illnesses, injuries, operations, and deformities suffered by the missing person, with the approximate dates of occurrence and the names of the hospitals and medical and dental attendants. Sometimes the characteristics of a missing person were so striking that

4. Grant, E. A.: Ontario Dental Journal, to be published.

5. Culbert, W. L., and Law, F. M.: Identification of a Body by Comparison of Roentgenograms of the Nasal Accessory Sinuses and Mastoid Processes, J. A. M. A. **88**: 1634 (May 21) 1927.

6. Dutra, F. R.: Identification of Person and Determination of Cause of Death from Skeletal Remains, Arch. Path. **38**: 339, 1944.

the body could be picked out easily. Oftener, however, the answers were indefinite and the details in the descriptions vague. From among the hazy recollections and the casual remarks of these distraught relatives, it required the knowledge of physicians to sift out the important clues and to ask the pertinent questions. These interviews with the relatives of a particular person were often

Fig. 1.—Body of a girl finally identified by the finding of a vaginal tampon.

repeated many times, because the relatives were usually unable to stand prolonged questioning. On the other hand, each interview brought out some new fact, and gradually, through persistent inquiry, a reasonably clear description of the person would evolve.

To complete all the different examinations of the bodies and interview most of the relatives of missing persons took up the first week, and, during this time, the first 59 bodies were identified. Relatively undamaged valuables and property on these bodies were recognized by the relatives. When the manifestations of old disease, operations, and physical defects were unmistakable at autopsy and could be clearly matched with the relatives' descriptions of these or the clinical records of the missing persons, there was little question as to the identification. Nor was there any with the comparison of the characteristic antemortem and postmortem dental charts, roentgenograms, and fingerprints. This large group of cases was the one in which the evidence on the body was easy to find, and in which the information on the missing persons was readily available and the comparisons obvious.

One of the more striking illustrations of these early identifications was that of three members of a family lost in the "Noronic" disaster. The father and mother were identified by a relative on the basis of his recognition of the appearance of the bodies and the personal property found on them, but the missing daughter could not be located. The dentist eliminated all but four from among the possibilities from the many female bodies, and the relatives picked out one particular body, which closely resembled that of the missing girl. The personal property on the body, a shoe and fragments of a nightgown, together with its general appearance, were consistent. Medical inquiry, however, brought out the fact that the missing girl was known to have had a scar over the right mastoid area, and to have been menstruating, whereas the identified body showed that a hysterectomy had been performed, and no mastoidectomy scar could be found. A subsequent investigation discovered a body of about the same build (Fig. 1), in which a vaginal tampon was discovered, and, which bore the scar of a right mastoidectomy. The relatives then positively identified this body as the missing girl. The shoes on the two bodies were the same size, and the color of the fragments of cloth on both bodies was identical, but one cloth had a figured pattern and the other, a polka dot pattern. These cases demonstrated the values and the dangers of recognition of property on bodies in identification, as well as the value of autopsies and the confirmatory nature of multiple evidence.

During the second week after the fire, when the obvious distinctive features on the bodies became scarce, the difficulties in identification began to arise. Nevertheless, while the records on the unsolved cases did not supply enough information to make identification simple, they contained everything known to our committee and were full of clues that had to be followed. With this information as a basis, each case was pursued. The bodies were repeatedly examined, and more sections for microscopic study and x-ray examinations were made. Interviews with relatives were repeated, and messages were sent to anyone who might have known anything about the missing person. Through the Canadian Red Cross teletype network, the inquiries were sent to hospitals, physicians, dentists, lawyers, banks, employers, business associates, and neighbors of the missing persons all over the United States. Trained Red Cross and social service

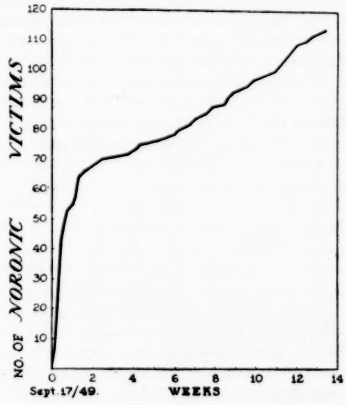

Fig. 2.—Progress of identification procedure.

workers in the United States, familiar with the local situation in these communities, bent every effort to track down the answers to our queries. Their comprehension of the problem and the thoroughness of their search were a major contribution to the investigation. As the replies came into the files, further questions were asked and amplifications sought. From the yards of teletype messages and the stacks of telegrams and letters, the salient

facts were laboriously culled and slowly fitted together to complete the patterns that established the identities. The procedure was tedious but effective, and at the end of the first month, 78 bodies were identified. The graph (Fig. 2) illustrates the rate of progress of the work.

There were still 42 bodies in the morgue, and, at that time, despite strenuous efforts, little headway had

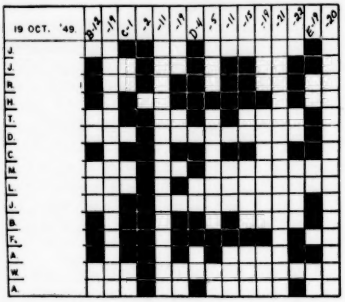

Fig. 3.—Sample of the "crossword puzzle" charts used early in the identification procedure. Horizontal squares indicate persons known to be "Noronic" victims; vertical squares represent "Noronic" bodies. Squares were blackened to indicate that the pairs did not match, and, later in the investigation, variously marked squares were used to show the means by which identification was made.

been made in their identification. There just was not enough information on them for the committee to proceed. It was, however, discovered that what was known about some of the cases made it impossible for the particular body to be that of more than a very few of the unidentified persons. To demonstrate the situation graphically, as applied to all the cases, two graphs were drawn, one for males, the other for females. The unidentified bodies were listed as the abscissa and the missing persons, as the ordinate. When a particular body was excluded as a possibility for a missing person, the square on the chart common to both was filled in black. When the charts were completed they looked like crossword puzzles and the possibilities for each body and each person still to be identified stood out clearly (Fig. 3).

When the chart for the men was completed, there was the name of one missing person (Mr. K.) from which all but five bodies had been excluded. Of these five, however, one of the bodies had been eliminated as being that of any other of the missing persons but Mr. K. At that time evidence from medical, dental, x-ray, and property examinations indicated that this body was the most likely possibility, but there was still not sufficient evidence to complete the identification. When the chart proved that all other bodies had been ruled out, the investigation was intensified. This was one body from which the fingerprints had been made. The relatives of the man in question were pressed for further information, and ultimately it was found that he had been fingerprinted at a factory during the war. Comparison of these patterns with those of the body under investigation was made by the F. B. I., and the identification was established. Although it was by the finger ridge patterns that the identification of this case was made, the antemortem fingerprints could not have been found unless other types of investigation had pointed definitely to this particular body. This illustrates how the crossword puzzle was put to use. It is to be stressed that elimination by the chart, as in this case, was never employed as the final evidence for identification. It was upon the positive evidence only that the identification was acceptable; the chart simply pointed out the bodies on which the efforts of the committee were to be concentrated in each case.

During the three months that were required to identify the remaining 23 cases, the exclusion charts were the keystone of the investigation. With the leads it gave, the examination of the bodies became more particular, and the inquiries about the missing persons more pointed. One case that illustrates the procedure at this stage was that of Mr. K. V. It was on the 23rd of November that we succeeded in identifying him. He had been the subject of an intensive search from the outset. He was known to have had an artificial left eye, but this could not be found in any of the bodies in the morgue. Chest roentgenograms taken in 1941 and 1943, had been destroyed, and the only film that was sent to us was that of an old fracture of the ankle, which could not be matched with any of the bodies. A great deal of correspondence on this case was carried on through the Canadian Red Cross teletype with a brother of K. V.'s. He returned to Toronto in November to see if he could not finally get some lead as to his brother's identity, and, during a conversation with one of our group, he casually mentioned that, at times, his brother would pass bloody urine. In the morgue there was one male body with bilateral polycystic kidney disease. This could have caused the intermittent hematuria, and it is known to be inherited. Mr. V.'s physician wrote that, while he had no evidence that K. V. had this condition, a brother had died of it, and that his father, a sister, a niece, and a nephew all had the disease. The

Fig. 4.—Body of a man who had worn an artificial eye. Identification was established by microscopic examination of the optic nerve.

body of the man (Fig. 4) who had cystic disease of the kidney was the same height as K. V., but this body had no artificial eye. The charred contents of both eye sockets were removed from this body, and it was found that the optic nerve on the left side was half the size of that on the right. Microscopic examination confirmed the atrophy of the left optic nerve (Fig. 5), and the degree

of atrophy was consistent with the history of old traumatic injury.

Four months after the fire the committee was left with three unidentified bodies and three unidentified missing persons. The files on all the cases contained a great deal of information, and, although it was not improbable that the three bodies were those of the three missing persons, there was not enough positive evidence. In these cases failure had to be conceded. The identification of the "Noronic" victims was therefore closed.

Before the files were closed on the "Noronic" disaster, the committee undertook a comparative review of the methods employed in identifying these badly burned bodies. Consideration of the relative value in the entire identification project of the different types of investigation substantiated the general impression that the results

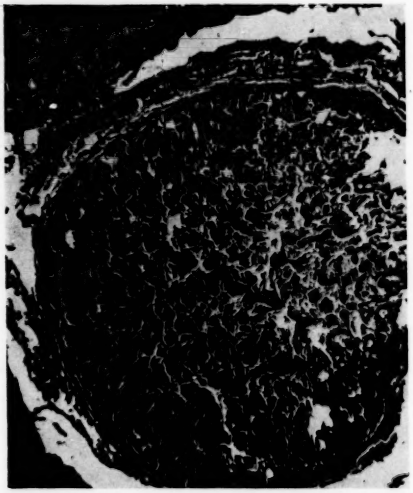

Fig. 5.—Photomicrograph showing section of abnormal optic nerve by which a victim was identified (Fig. 4).

achieved were due to the cooperation among all those involved. The most important evidence for the identification was contributed by the recognition of property and valuables in 32 cases, by dental studies in 25, by roentgenogram comparisons in 19, by pathology and medical histories in 16, and by fingerprints in 6 cases. In 10 cases property and valuables were the only evidence, and the dental findings were the sole basis for identification in 4 cases. In only one case did the medical evidence alone prove the identity. It would appear that property and dental studies were preeminent, but this deduction must be modified with respect to the following facts. The investigation of each case was closed when sufficient evidence for identification was produced. In the last 42 cases, the really difficult ones, which were the subject of the most prolonged search, autopsy and x-ray were the most important factors in identification in nine instances each, whereas dental evidence was of value in only three, and property in only two. No matter how these figures reflect the relative merits of the different identification methods, they deal only with the solution of a small number of cases, and this review did disclose that in the majority of cases the different modes of study made their significant contributions when used in conjunction with each other. Dental evidence was used in 72 cases, autopsy in 70, property in 53, roentgenograms in 38, and fingerprints in 13. In 50 cases the assistance of the Canadian and American Red Cross was a major contribution. It is obvious, therefore, that no one form of examination could have resolved this situation by itself, but, on the other hand, the combined efforts of all these different groups met with almost perfect results.

In this general account of the medical aspects of the "Noronic" identification, further observations on all the different types of investigation must, of necessity, have a bearing on the scheme as a whole, and yet to enlarge on them would be beyond the scope of this report. Indeed, the radiologists,[7] the dentists,[4] the dactylographers,[8] the police, and the Red Cross [9] either have reported or are on the point of publishing their methods and experiences, and the full particulars are to be found in their special periodicals. However, as the radiological study is new and falls within the realms of medicine, it is permissible to comment briefly upon it. Antemortem films on 35 of the missing persons were received, and, by comparison with the roentgenograms of the bodies, 24 positive identifications were made. Confirmatory but inconclusive evidence was forthcoming in five more cases. The limitations of this method have already been alluded to, and the destruction of bony details by fire and the necessity for antemortem films are the important ones. Within these bounds, however, identification by roentgenogram comparison has been established as an absolute criterion. The pathologists acted as coordinators of the entire project and took full charge of the mortuary and the investigation, thereby suppressing the chaotic tendencies of the situation in its earlier hours. For the first three weeks every department in the committee was fully occupied in making successful identifications with the evidence they were producing, but, as the problems became more difficult and their solutions seemed unlikely, the pathologists, by repeatedly probing every bit of information, provided the stimulus and the momentum that carried the project to its conclusion.

In the retrospective consideration of the "Noronic" studies, an account of the mistakes by the committee is as enlightening as its successes. In the identification of the dead there are always a number of pitfalls to be avoided, and, when so many mutilated bodies are concerned, these difficulties are multiplied. Although the Medical Identification Committee was aware of many of these, almost all of them were encountered, and mis-

7. Singleton, A. C.: Roentgenological Identification of Victims of the Noronic Disaster, Am. J. Roentgenol. **66**: 375, 1951.

8. Borland, O. E.: Identification in the Noronic Disaster, Proceedings of the International Association for Identification in its 35th Annual Convention, 1950, Youngstown, Ohio, United Printing Company.

9. National Disaster Institute, Canadian Red Cross, Toronto, 1949.

takes were made owing to failure to recognize them, or because circumstances made such mistakes unavoidable. A number of mistakes had already been made before the committee was organized. The removal of the bodies from the ship without taking a record of the site on the ship where the body was found was a definite mistake in technique, and yet, at the time, such documentation would not have been practical and, in the final analysis, no harm was done to the scheme. Admitting relatives to the mortuary, and permitting them to handle the bodies and property without proper supervision was another mistake that had to be rectified by the Medical Identification Committee. Nothing was gained by allowing the relatives to roam among these badly burned bodies. Two of the cases illustrate how the Medical Identification Committee paid the high cost of experience. The first is that of the body of a man who was identified by his two sons purely on their supposed recognition of a chip in a denture taken from the body. This happened on the day after the fire, just as the committee was starting its work. After the body had arrived for burial in Detroit, fingerprint studies were made, and they pointed out an error in identification. This body had to be returned to the mortuary. The correct body for this particular missing person was found shortly afterward. The dental features, the physical features, including an indirect inguinal hernia, and the fingerprints all proved the correct identification. This mistake illustrated not only the value of taking time to check the fingerprint studies but also the fallacy of accepting the recognition of relatives of mutilated bodies. In a second case the death certificate was issued for a woman missing in the fire on the basis of the finding of her social security card and the keys to her house, together with a portion of an arm at the site of the cabin on the ship which she occupied. Later, when her body was identified, there was considerable reluctance on the part of the family to accept the identification, mainly because they had already conducted a funeral for this person. The identification of this particular body was actually delayed by a mistake in taking for granted that parts of bodies belonged with a body near which they were found. While medical, dental, x-ray, and property evidence all were consistent with the identification of the particular woman, fingerprint evidence was repeatedly at odds, until it was discovered that the fingerprints were made from the hand that was with the body, but not attached to it. Actually the body from which the hand had come had been previously identified as somebody else. Such mistakes would seem easy to forestall, and yet, in the disturbed atmosphere under which the whole "Noronic" disaster investigation had to be conducted, they were inevitable. The commoner mistakes were made when the Identification Committee was rushed by situations beyond its control, and, as the errors came to light, the jurisdiction of the Identification Committee was strengthened, and interferences disappeared.

SUMMARY AND CONCLUSIONS

The identification of all but 3 of 119 persons who died in the fire that gutted the steamship "Noronic" represents an outstanding achievement, and the arduous medical investigation by which it was accomplished has no precedent. Most of the bodies were absolutely unrecognizable. The facial features were wiped out, the skin was burned away, many limbs were missing, the viscera were shrivelled, and the clothing frazzled. So severely damaged were the bodies that few distinguishing characteristics remained, and the difficulties to be resolved far exceeded the capacity of the accepted procedures in the science of identification. These problems required a much broader approach, the basis of which was the comparison of all the information gathered on the missing persons with the facts gained by examination of the bodies. The responsibility for the collection and the complex analyses of the disaster rested on the pathologist.

The crossword puzzle charts and the other methods they developed for the utilization of this information were the key to the ultimate success of the project. The ordinary techniques in the science of identification were made use of, and an addition to the armamentarium was developed when the comparison of roentgenograms of the bodies with those of the missing persons proved their identity beyond question. Recognition of property on the bodies, fingerprint studies of the F. B. I. and the Toronto police, the autopsies and the medical inquiries of the pathologists, examinations made by the dentists—all were signal contributions to the identification, but it was through a combined effort of the entire Medical Identification Committee that the results were obtained. Teletype communication with centers throughout the United States and Canada, provided by the Red Cross, and the assistance they gave in all phases of the investigation, were an asset without which the project could never have been completed.

The Medical Identification Committee for the "Noronic" disaster has demonstrated that, no matter how badly charred or mutilated human bodies may be, their identity can be established by careful and prolonged medical investigation.

100 College St. (Dr. Brown).

New Problems in Treatment of Infectious Diseases.—Among the problems which confront us in the treatment of infections today, the following seem to be the most important: First is the increasing prevalence of infections caused by bacteria resistant to our present antibiotic drugs. This increase has not occurred in all bacterial infections. The most striking and most disturbing is the rising incidence of penicillin-resistant staphylococcal infections. This increase is thought to be due to the gradual reduction in numbers of naturally sensitive strains, rather than to the development of acquired resistance. A second problem is the occasional occurrence during antibiotic therapy of complicating infections caused by bacteria insensitive to the antibiotic being used, sometimes by microorganisms usually regarded as nonpathogenic. When such infections begin, for example, in the pharynx, they may result from a change in the bacterial flora of the throat, that is to say, from a disturbance of the equilibrium maintained by the bacterial antagonisms within the normal flora. Finally, infection may become a serious complication during treatment with ACTH or cortisone, presumably because these drugs interfere with the host's defensive response to bacterial invasion.—C. Phillip Miller, M.D., New Problems in the Treatment of Infectious Diseases, *Annals of Internal Medicine*, October, 1951.

EFFECT OF ACTH AND CORTISONE ON RHEUMATIC CARDITIS

OBSERVATIONS ON EIGHTEEN CASES

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and
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In May, 1949, Hench and his co-workers [1] published their first paper on the treatment of acute rheumatic fever with cortisone and corticotropin (ACTH). These authors found that the effect on fever, polyarthritis, general "toxicity," and the erythrocyte sedimentation rate was striking, and these results have now been amply confirmed.[2] In this preliminary report Hench and his associates stated that the effect on rheumatic carditis was difficult to evaluate. In the opinion of those authors, patients receiving hormone therapy would have to be observed for many months before it could be determined whether chronic organic injury to the heart valves or myocardium had been prevented or decreased.

PLAN OF STUDY

In order to determine the effect of corticotropin and cortisone on rheumatic carditis, patients with rheumatic fever who had definite symptoms and signs of cardiac involvement were selected. The results obtained in 16 children, 1 adolescent, and 1 adult are reported. Twelve of these 18 patients were admitted during their first attack, and 6 gave a history of one or more antecedent rheumatic episodes.

Criteria for the Diagnosis of Carditis.—The diagnosis was made on the basis of the presence of one or more of the following symptoms: pericardial friction rub or effusion, roentgenographic evidence of change in the size or contour of the heart, congestive failure in children, the appearance of new murmurs, heart sounds of poor quality, gallop rhythm, and tachycardia in the absence of fever. None of the patients included in this report had a significant prolongation of the PR interval.

Therapeutic Regimen.—Four of the 18 patients received a single course of corticotropin (Cases 1, 3, 14, and 16), and 2 patients (Cases 6 and 8), a single course of cortisone. It was found that the acute symptoms of rheumatic fever (fever, "toxicity," and polyarthritis) subsided more quickly with corticotropin than with cortisone (throughout this study cortisone was administered by intramuscular injection). On the other hand, side-effects such as retention of sodium and water and loss of potassium were less marked in patients receiving cortisone. In four instances, therefore, corticotropin was given for three or four days and then followed by a longer course of cortisone (Cases 2, 4, 7, and 11). Patients who had relapses or failed to respond to cortisone were given one or two courses of corticotropin (Cases 9, 12, 13, and 18). One patient (Case 10), who showed only slight improvement after one course of corticotropin was given a second course for four days, followed by cortisone for 23 days. One patient (Case 15), who showed sodium and water retention after 16 days of corticotropin therapy, was changed to cortisone.

The eosinophil response was studied both in patients receiving corticotropin and in those receiving cortisone. A count was made before therapy was begun and approximately four hours after the initial injection of the hormone. A reduction of more than 50% in the number of eosinophils was obtained in the 15 cases in which it was studied. The range in the number of eosinophils was then followed throughout the period of therapy. The eosinophil response to cortisone was of the same order of magnitude as that to corticotropin.

Criteria for Evaluating the Effect of Hormone Therapy on Carditis.—An attempt was made to analyze the effect on the various aspects of cardiac involvement, including pericarditis, myocarditis, and endocarditis. In pericarditis the well-established criteria for improvement are disappearance of the pericardial friction rub, change in contour of the cardiac silhouette on roentgenographic examination, return of elevated ST segments to the isoelectric position, and the reversion of the T wave to normal in the electrocardiogram. Decrease in endocarditis due to valvular inflammation is indicated by the disappearance of newly developed murmurs or by a reduction in the intensity and transmission of the mitral systolic murmur. Objective findings of subsiding myocarditis are a roentgenologic decrease in the size of the heart in the absence of pericardial effusion and in children the disappearance of signs of congestive failure, with or without digitalization and diuretics. Congestive failure due to severe rheumatic infections, in contrast to that caused by mechanical

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Dr. Harrison F. Wood of the Rockefeller Institute supplied the immune rabbit serum used for the C-reactive protein test.

The case protocols have been omitted from THE JOURNAL for lack of space but are included in an appendix to the authors' reprints.

Many of these cases were referred by Dr. Marcus Kogel, Commissioner of Hospitals, New York City, and staff physicians of hospitals in Greater New York.

This study was aided by grants from the Masonic Foundation for Medical Research and Human Welfare, the Helen Hay Whitney Foundation, and the New York Heart Association.

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factors, often fails to respond to digitalis and mercurials. Other findings, some of which are more subjective, include an improvement in the quality of heart sounds and a reduction in what is usually described as cardiac "overactivity," indicated by the disappearance of gallop rhythm and tachycardia and a decrease in the lability of the cardiac rate.

RESULTS

For purposes of evaluation the 12 patients treated during their first rheumatic attack were divided into three groups. Group 1 received hormone therapy 8 to 14 days following the onset of rheumatic manifestations, Group 2 received therapy 35 to 52 days after onset, and Group 3 had had active or low-grade rheumatic fever for periods varying from 2 to eight months before receiving therapy. Since the results obtained in Groups 1 and 2 are similar, data on the eight cases included in these two groups are presented in Table 1 and on Group 3 in Table 2. The treatment was continued more than six weeks. L. Z., on the other hand, was not acutely ill. He had apical systolic and diastolic murmurs, tachycardia, heart sounds of poor quality, and a labile cardiac rate. In addition to carditis he had mild chorea. During the first week of treatment tachycardia subsided, and the heart sounds improved but did not become normal. The lability of the cardiac rate persisted, and there was no change in the murmurs. The choreiform movements subsided completely. During the second and third weeks of therapy there was no further improvement in the carditis, and administration of corticotropin was therefore discontinued. Signs of activity then decreased gradually, the apical diastolic murmur disappeared eight weeks after treatment was stopped, and the rheumatic process was considered to be inactive.

B. L. (Case 4) was the youngest and most critically ill patient in Group 1. She had severe congestive failure,

TABLE 1.—*Eight Patients Receiving Hormone Therapy Eight to Fifty-two Days After Onset of First Attack*

Case	Age, Yr.	Days from Onset to Treatment	Therapy: Hormone *	Therapy: Days Treated	Therapy: Total Dose, Mg.	Therapy: Maximum Daily Dose, Mg.	Active Carditis: Persistence of, or Time Required for Subsidence: During Therapy	Active Carditis: Persistence of, or Time Required for Subsidence: After Therapy	Follow-up: After Therapy, Mo.	Follow-up: Cardiac Status §
Group 1										
1.	9	8	ACTH	46	1,160	60	2 wk.	Inactive	9	Inactive; EH, MI
2.	4	9	ACTH	3	180	60	4 wk.	Inactive	5	Inactive; Sl EH, MI
			Cortisone	34	3,250	100				
3.	5	14	ACTH	21	935	60	Active	8 wk.	7	Inactive; Sl EH, MI
4.	2	14	ACTH	4	180	60	Active	9 wk.	5	Inactive; EH, MI, MS
			Cortisone	42	7,100	200				
Group 2										
5.	8	35	ACTH	23	970	60	3 wk.	Inactive	7	Inactive; Sl EH, MI, AI
6.	7	35	Cortisone	47	4,425	100 †	3 wk.	Inactive	2	Inactive; EH, MI, MS
7.	7	39	ACTH	3	300	100	Active	6 wk.	4	Inactive; EH, MI, MS, AI
			Cortisone	48	7,750	200				
8.	3	52	Cortisone	27	2,640	100 ‡	Active	8 wk.	7	Inactive; EH, MI

* ACTH = corticotropin.
† This patient received 300 mg. on the first day and 200 mg. on the second day.
‡ This patient received 200 mg. on the first day.
§ Sl. = slightly; EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency.

courses of the six patients who had a history of previous rheumatic attacks are presented in Table 3 and are arranged according to the length of time that elapsed from onset to treatment.

Brief summaries of each case appear in the appendix. Only pertinent laboratory data, such as the C-reactive protein test,[3] the erythrocyte sedimentation rate (Westergren), the eosinophil response to the first injection of hormone, the range in the number of eosinophils during therapy, and the roentgenographic findings, are included. More detailed reports and discussion of the effects of corticotropin and cortisone on the erythrocyte sedimentation rate and on the C-reactive protein response are reported elsewhere.[4]

Group 1.—The first four patients shown in Table 1 were treated within 14 days or less of the onset of the first attack of rheumatic fever. C. M. and L. Z. (Cases 1 and 3) both received corticotropin. In the former carditis subsided during therapy, whereas in the latter activity persisted. C. M. was acutely ill with pericarditis and severe extensive polyarthritis, and, although the carditis became inactive after two weeks of therapy, which subsided only after digitalis and meralluride injection (mercuhydrin sodium solution*) were added to hormone therapy. In this patient hormone therapy was considered a lifesaving measure, because in a child of this age digitalis and meralluride injection often fail to control heart failure. This child received a total of 180 mg. of corticotropin and over 7 gm. of cortisone, yet, in spite of a prolonged period of treatment and high dosage, active carditis persisted. Therapy was discontinued because of the marked side-effects of fluid retention, abdominal distention, adiposity, and furunculosis. Six weeks after treatment was stopped, in addition to the apical systolic murmur that was present on admission, an apical diastolic murmur became audible and has

3. Anderson, H. C., and McCarthy, M.: Determination of C-Reactive Protein in the Blood as a Measure of the Activity of the Disease Process in Acute Rheumatic Fever, Am. J. Med. **8**: 445 (April) 1950.

4. (*a*) Fearnley, G., and Bunim, J. J.: The Effect of ACTH and Cortisone on Sedimentation Rate and Fibrinogen Content of Blood, in Mote, J. R., Proceedings of the Second Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1951. (*b*) Ziegra, S. R., and Kuttner, A. G.: Reappearance of Abnormal Laboratory Findings in Rheumatic Patients Following Withdrawal of ACTH or Cortisone (with Special Reference to the C-Reactive Protein), Am. J. M. Sc. **222**: 516 (Nov.) 1951.

persisted. The rheumatic process remained active eight weeks after therapy was discontinued. The follow-up examinations five to nine months after treatment was discontinued show that hormone therapy, instituted shortly after onset of the first rheumatic attack, had failed to prevent organic heart disease in the first four patients in this group. Three had definite and one questionable cardiac enlargement.

Group 2.—As far as subsidence of rheumatic activity was concerned, essentially similar results were obtained in the children included in Group 1 and in Group 2. In two of the patients carditis subsided during therapy, and in two it persisted for six to eight weeks after treatment was discontinued. Patient V. D. (Case 5) was acutely and critically ill with pericarditis and congestive failure. A dramatic response was obtained with corticotropin. Congestive failure subsided without digitalis or mercurials, and the rheumatic process became inactive within three weeks. Patients K. S. and D. E. (Cases 6 and 8), in contrast to patient V. D., were not acutely ill. In patient D. E. rheumatic activity did not subside with therapy. During the first eight days of treatment tachycardia decreased and the quality of heart sounds improved but did not become normal. Tachycardia and lability of the cardiac rate persisted. After 27 days therapy was stopped because there was no further improvement and severe furunculosis had developed. Carditis subsided gradually, and eight weeks later the rheumatic process was considered to be inactive. In Case 6 carditis subsided more rapidly, and it is possible that a similar result might have been obtained in Case 8 if larger doses had been used.

Patient J. M. (Case 7) was acutely ill. He had erythema marginatum, apical systolic and diastolic murmurs, an inconstant aortic diastolic murmur, and multiple nodules. He was given corticotropin during the first three days, followed by cortisone for 46 days. The nodules decreased in size and number in 10 days, but a few small nodules persisted more than six weeks. In spite of large dosage, rheumatic activity persisted with therapy. There was no change in the apical systolic and diastolic murmurs, and the aortic diastolic murmur became consistently audible. Moon face and fluid retention with scrotal edema developed, and therapy was discontinued. Activity gradually subsided six weeks after treatment was stopped. In this patient biopsies of nodules were taken before treatment and after 38 days of therapy. A comparison of the sections of these two nodules showed a striking difference; the nodule obtained before treatment showed confluent small areas of granulomatous inflammation characterized by infiltration of pleomorphic mononuclear cells, minute focal areas of altered collagen, and the formation of new blood vessels. The nodule obtained after treatment showed very prominent areas of altered collagen and almost no cellular reaction.

The follow-up examinations of the four patients in Group 2 two to seven months after treatment showed that hormone therapy administered during the course of their first attack of rheumatic fever had failed to prevent organic heart disease. In Group 2, in contrast to Group 1, however, therapy was not instituted until five to seven and one-half weeks after onset, and it seems possible that during this interval the rheumatic infection may have caused irreversible damage. As shown in Table 1 the valvular lesions resulting from rheumatic carditis were severer in Group 2 than in Group 1.

Group 3.—The first attacks of rheumatic fever in the four patients of Group 3 presented in Table 2 were characterized by continuously active or low-grade rheumatic fever of two to eight months' duration prior to treatment. The response to hormone therapy in this group was less pronounced than in the patients treated earlier in the course of their disease (Table 1).

TABLE 2.—*Four Patients Treated Two to Eight Months After Onset of First Rheumatic Attack*

Case	Age, Yr.	Days from Onset to Treatment	Therapy: Hormone *	Therapy: Days Treated	Therapy: Total Dose, Mg.	Therapy: Maximum Daily Dose, Mg.	Active Carditis: Persistence of, or Time Required for Subsidence: During Therapy	Active Carditis: Persistence of, or Time Required for Subsidence: After Therapy	Follow-up: After Therapy, Mo.	Follow-up: Cardiac Status §
Group 3										
9	8	61	Cortisone	7 † (Relapse after 12 days; re-treated after 17 days)	875	150	Active	Active	14	Inactive; EH, MI, MS, AI
			ACTH	32	1,360	100	Active	7 wk.	..	.....
10	13	90	ACTH	38 (No improvement; re-treated after 12 days)	1,460	75	Active	Active	4	Inactive; Mod EH, MI, MS, AI
			ACTH	4	300	100	Active	5 wk.	..	.....
			Cortisone	23	3,000	200				
11	6	105	ACTH	3	180	60	Active	Active	4	Inactive; EH, MI, AI
			Cortisone	26 (No improvement; re-treated after 7 days)	3,000	200				
			ACTH	31 (Rebound after 3 days; subsided without treatment)	5,560	250	Active	7 wk.	..	.....
12	5	240	Cortisone	27 (No improvement; re-treated after 14 days)	2,000	100 ‡	Active	Active	3	Active; EH, MI, MS
			ACTH	10 (No improvement; re-treated after 32 days)	835	100	Active	Active	..	.....
			ACTH	28	4,060	320	Active	Active	..	.....

* ACTH = corticotropin.
† Cortisone discontinued because of increasing heart failure.
‡ This patient received 200 mg. on the first day.
§ EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency.

In the first of these four patients therapy was discontinued after seven days because fluid retention developed and heart failure increased. This patient's congestive failure was controlled with meralluride injection. Twelve days later he relapsed and was re-treated. Signs of active carditis persisted during the second course of therapy and did not subside until seven weeks after treatment had been stopped. In two children, although they were treated for 38 and 29 days, respectively, sleeping pulse rate again rose sharply. That the rheumatic process was still very active was indicated by the fact that the results of the C-reactive protein test, which had become negative while the patient was receiving 320 mg. of corticotropin daily, again became strongly positive five days after therapy was discontinued.

The follow-up examinations three to fourteen months after therapy was discontinued showed that these four patients had organic heart disease. However, in spite of

TABLE 3.—*Six Patients with Histories of Previous Rheumatic Attacks Treated 6 to 280 Days After Onset of Current Attack*

Case	Age, Yr.	Previous Attacks	Cardiac Diagnosis on Admission *	Days from Onset to Treatment	Therapy: Medicament †	Days Treated	Total Dose, Mg.	Max. Daily Dose, Mg.	Active Carditis Persistence of, or Time Required for, Subsidence, Weeks: During Therapy	After Therapy	Follow-Up: After Therapy, Mo.	Cardiac Status *
13	12	2	Mod. EH, MI, MS, AI, AS	6	Cortisone	44	4,500	100	3	Active	..	.....
					(Relapse after 10 days; re-treated after 12 days)							
					ACTH	4	300	100	Active	10	4	Inactive; Mod. EH, MI, MS, AI, AS
					Cortisone	17	2,500	200				
14	9	1	Sl. EH, MI, MS	11	ACTH	9 ‡	540	80	Active	8	5	Inactive; Sl. EH, MI, MS
15	20	1	Mod. EH, MI, MS	13	ACTH	16	1,265	100	Active	Active	3	Active; Mod. EH, MI, MS
					Cortisone	28	3,875	200				
16	12	1	Mod. EH, MI, MS	23	ACTH	52	2,145	60	Active	8	7	Inactive; Mod. EH, MI, MS
17	15	10 §	Sl. EH, MI	37	ACTH	3	300	100	Inactive	Active	..	.....
					Cortisone	17	2,800	200				
					(Relapse after 8 days)							
					Sod. salicyl.	23	.....	9,000	1	Inactive	..	.....
18	9	2	Marked EH, MI, MS	270	Cortisone	26	1,630	100	Active	Active	..	Active; marked EH, MI, MS
					(No improvement; re-treated after 36 days)							
					ACTH	13	520	40	Active	Active	12	.....

* Mod. = moderately; Sl. = slightly; EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency; AS = aortic stenosis.
† ACTH = corticotropin; Sod. salicyl. = sodium salicylate.
‡ Discharged at mother's request.
§ One attack of carditis followed by multiple attacks of mild polyarthritis.

TABLE 4.—*Effects of Hormone Therapy on the Signs of Carditis*

Case	Initial Attacks: 1	2	3	4	5	6	7	8	9 †	10 †	11 †	12 ††	Recurrent Attacks: 13 †	14	15	16	17 §	18
Pericarditis	A	...	...	...	A	A	...	...	A	...	...	...	A	A	A	A	...	A
Congestive failure	...	A	...	A	A	...	...	...	A	...	...	A	...	...	...	...	...	AP
Cardiac enlargement *	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	A	AP
Murmurs																		
Mitral systolic	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP
Mitral diastolic	...	...	AP	...	A	AP	AP	...	AP	AP	A	AP	AP	AP	AP	AP	...	...
Aortic diastolic	...	...	...	...	AP	...	AP	...	AP	AP	AP	...	AP	...	...	...	AP	...
Aortic systolic	...	...	...	...	...	...	...	...	...	...	...	...	AP	...	...	...	...	...
Poor quality heart sound	A	A	AP	AP	A	A	A	AP	A	A	A	AP	A	AP	A	A	...	AP
"Overactivity"																		
Gallop	...	A	...	A	A	A	A	...	A	AP	A	AP	...	A	A	...	A	...
Tachycardia	A	A	A	AP	A	A	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	...	AP
Labile rate	A	A	AP	AP	A	A	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	...	AP
Nodules	...	...	...	...	...	...	A	...	A	A	...	...	...	...	...	...	...	...

A = Finding present before therapy.
P = Finding still present three weeks after complete cessation of therapy.
* Enlargement exclusive of that due to pericardial effusion.
† These patients received two courses of hormone therapy.
†† This patient received three courses of hormone therapy.
§ This patient received one course of hormone therapy and one course of salicylate therapy.

carditis persisted and they were therefore given a second course of therapy. In both these children signs of active carditis did not subside until several weeks after the second course had been discontinued. In the fourth patient carditis persisted during three separate courses of therapy. Because no response was obtained with the first two courses, massive doses of corticotropin (320 mg. daily) were tried. With this dosage the sleeping pulse of this patient became normal for the first time. However, severe side-effects, including moon face, abdominal distention, adiposity, hyperpigmentation, and hirsutism, developed. Corticotropin, therefore, was gradually reduced to 60 mg. daily. With this dose the the prolonged period during which active carditis had persisted in these patients there was no further increase in the size of the heart.

Patients with Previous Rheumatic Attacks.—Three of the patients who had histories of previous rheumatic episodes (Table 3) were treated within 13 days or less of onset of their current attack. In patient P. L. (Case 13) carditis appeared to have become inactive after three weeks of therapy. Treatment was continued for an additional three weeks. Ten days after therapy was discontinued, however, a severe relapse of carditis and polyarthritis developed. A second course of therapy was given during which, in contrast to the first, carditis per-

sisted. Therapy was discontinued after 20 days because there was no progressive improvement and pronounced side-effects had developed. Carditis then subsided gradually and was considered to be inactive 10 weeks after treatment was stopped. V. S. (Case 15) received corticotropin for 16 days and was then changed to cortisone because of fluid retention. In patient H. C. (Case 17) carditis was considered to have become inactive after 20 days of treatment, and therapy was therefore discontinued. Eight days later, however, a relapse of polyarthritis developed, which subsided promptly with salicylate therapy. There was no recurrence of carditis, and the rheumatic process was considered to be inactive after 23 days, when administration of sodium salicylate was discontinued. Patient M. B. (Case 18) had had severe

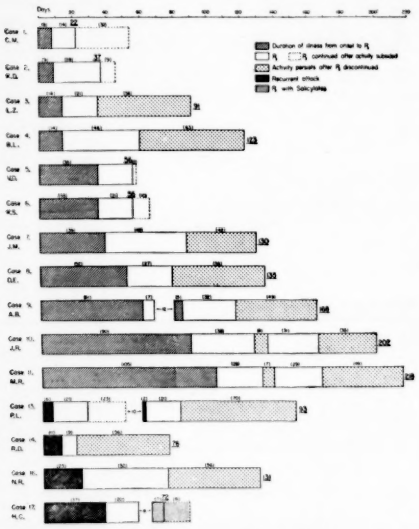

Chart showing course of 15 patients in whom carditis became inactive during or following treatment with cortisone or corticotropin.

polycyclic carditis for eight months prior to admission. Hormone therapy was instituted because of an acute exacerbation that increased the congestive failure. In the light of our subsequent experience, considering the severity and duration of the symptoms in this case, the dosage of both cortisone and corticotropin was probably inadequate. Laboratory as well as clinical evidence of continued rheumatic activity persisted during both courses of therapy.

Immediate Effect on Carditis.—The effect of hormone therapy on the persistence or subsidence of the various manifestations of carditis in the 18 cases reported in this paper is summarized in Table 4. The results were evaluated three weeks after complete cessation of therapy. This period of time was considered adequate to allow for the possible occurrence of symptoms due merely to the withdrawal of hormones. As shown in Table 4 the two aspects of carditis that apparently responded favorably to hormone therapy were pericarditis and congestive failure. The one patient (Case 18) in whom cardiac decompensation did not disappear on therapy had severe heart disease with marked cardiac enlargement. This patient's C-reactive protein test and erythrocyte sedimentation rate did not become normal with therapy, suggesting that larger doses should have been tried.

In the absence of pericardial effusion, none of the 12 patients treated during their first attack of rheumatic fever showed a decrease in heart size. This was true in patients in whom the signs of carditis subsided during therapy as well as in those in whom rheumatic activity decreased gradually after therapy had been discontinued. In the group of patients who had had previous rheumatic attacks it was impossible to be sure that cardiac enlargement had not been caused by preceding rheumatic episodes. Aside from slight decrease in size attributed to the reabsorption of pericardial effusions, with one exception (Case 17), no significant change in cardiac enlargement was observed. A slight but definite decrease in size was noted in Case 17 after one week of therapy.

There was little change in the murmurs in the group of children treated during their first attack. Two children lost apical mid-diastolic murmurs, but in both these patients (Cases 5 and 11) aortic diastolic murmurs persisted. The murmurs remained unchanged in the six patients who had a history of previous rheumatic attacks or well-established rheumatic heart disease on admission.

The quality of the heart sounds in most instances showed a definite improvement during therapy. In 6 of the 18 cases, although the heart sounds improved, they were not considered to be normal three weeks after therapy was discontinued. In most patients gallop rhythm disappeared rapidly. Tachycardia in the absence of fever and lability of the cardiac rate were the signs of carditis that persisted most frequently.

Effect on Nodules.—Three of the 18 patients had nodules. In Case 7 the number and size of the nodules decreased in 10 days. However, a few small nodules persisted for more than six weeks. A. B. (Case 9) had only two small nodules, which had almost disappeared before therapy was begun. J. R. (Case 10) had numerous nodules, which had been decreasing in size and number for two weeks prior to admission. All the nodules disappeared in 10 days with therapy. Although their disappearance appeared to be accelerated, it was impossible to be sure that the nodules might not have disappeared in the same length of time without hormone therapy.

Rebound Phenomena.—In spite of the fact that the doses of corticotropin and cortisone were reduced gradually, most of the patients showed an increased erythrocyte sedimentation rate and in many instances results of the C-reactive protein test also became positive again shortly after therapy was discontinued. These abnormal laboratory findings subsided without further treatment within a period of three weeks.[4b] In one patient (Case 11) fever developed after the second course of therapy, but this also subsided spontaneously.

Side-Effects.—With the exception of one patient who was treated for only nine days, all the patients showed some signs of hyperadrenalism. These side-effects occurred with both corticotropin and cortisone and were

most marked in patients receiving prolonged treatment or massive doses. Moon face, acneform eruption, abdominal distention, adiposity, furunculosis, and fluid retention were observed most frequently. Striae and hirsutism were less common. Transient tremors that subsided while therapy was continued developed in three patients. Hyperpigmentation developed in one child while he was receiving massive doses. Aside from mild insomnia in one child, no mental symptoms developed. All the side-effects were reversible and disappeared gradually after cessation of therapy.

COMMENT

The value of corticotropin and cortisone in the treatment of rheumatic fever can be determined first by its immediate effect on the manifestations of carditis and second by a long-range study to determine whether ultimate cardiac damage is prevented or its extent decreased. In accord with the observations of other workers, it was found that corticotropin and cortisone produced a prompt improvement in the general condition of the patients. The temperature decreased, "toxicity" disappeared, and joint manifestations subsided. Various abnormal laboratory findings (results of the C-reactive protein test, the erythrocyte sedimentation rate, and gamma globulin) tended to become normal. These effects were most striking in acutely ill, febrile patients. They were obtained with both corticotropin and cortisone but occurred more quickly with corticotropin.

In this series of 18 cases the manifestations of carditis that apparently responded most favorably were pericarditis and congestive failure precipitated by severe rheumatic myocarditis. In evaluating any new therapeutic agent in the treatment of rheumatic fever, however, the great variability of the disease must be borne in mind constantly. Although our data suggest that pericarditis was favorably affected by corticotropin and cortisone, the persistence of this manifestation of rheumatic carditis is known to be extremely variable. In this series, therefore, we are not certain that the disappearance of pericarditis was accelerated.

For many years there has been a divergence of opinion in regard to the treatment of congestive failure occurring during the course of rheumatic fever. In such cases often little or no response is obtained with salicylates, and many observers believe that digitalis is of doubtful value. Six of our 18 patients had signs of heart failure, which in 5 instances subsided during therapy. Two of these six children were critically ill, and it was our impression that in these two patients hormone therapy had been a lifesaving measure.

Disappearance of gallop rhythm and improvement in the quality of the heart sounds were observed in most of our cases. Tachycardia in the absence of fever and lability of the cardiac rate were the two signs of carditis that showed the least response to hormone therapy. In this series of patients disappearance of murmurs and a decrease in cardiac enlargement, exclusive of that due to reabsorption of pericardial fluid, were rarely observed.

It was often difficult in acutely ill patients to evaluate to what extent changes in the cardiac findings were due to the antipyretic effect of corticotropin or cortisone. With the subsidence of fever, tachycardia usually decreased, and with the slowing of the cardiac rate the quality of the heart sounds tended to improve and gallop rhythm often disappeared. In patients with carditis who were afebrile or had only low-grade fever, the immediate response to hormone therapy was less marked than in acutely ill patients. Even in the absence of fever large doses of corticotropin and cortisone may induce bradycardia.[1] This effect is well illustrated in patient J. H. (Case 12). Only during his third course of treatment, while he was receiving massive doses of corticotropin (320 mg. daily), did his cardiac rate become normal for the first time, but as the dosage was decreased the tachycardia recurred.

In this series the length of treatment and dosage varied. Even in the cases in which relatively small amounts of corticotropin or cortisone were given, a reduction of more than 50% in the eosinophil count was obtained. In many instances therapy was discontinued, in spite of the fact that the carditis was considered to be active, either because there was no progressive clinical improvement or because of untoward reactions to the hormones. It is our impression that, if dosage is adequate to control fever and reduce the results of the laboratory tests indicative of inflammation (C-reactive protein test and the erythrocyte sedimentation rate) to normal, there is probably no advantage in using massive doses. The severity of the untoward reactions increased when very large doses were used. The rheumatic process subsided gradually over a varying period of time in most of the patients in whom carditis was considered to be active at the time therapy was discontinued. On the other hand, two patients whose rheumatic process was thought to have become inactive during therapy relapsed promptly when treatment was stopped. In one of these patients (Case 13), although treatment had been continued 44 days, carditis after relapse remained active during the second course of treatment and only subsided 10 weeks after therapy was finally discontinued. These observations suggest that the subsidence of rheumatic activity may have been a function of time rather than a direct effect of the hormones on the rheumatic process.

After an average period of six months following cessation of therapy in the 12 patients in this series treated during their first attack of rheumatic fever, lesions indicative of organic heart disease are still present. This is true in the four children receiving therapy within 14 days or less of onset as well as in those treated later in the course of their disease. Many more patients and longer periods of observation are needed to determine whether in less acutely ill patients corticotropin and cortisone significantly shorten the duration of carditis. Corticotropin and cortisone are known to suppress the inflammatory reaction to a variety of infective agents. It seems possible that in rheumatic fever these hormones, by suppressing the cellular reaction, may decrease the fibrotic scarring of the myocardium and endocardium. Furthermore, with improvement in the general condition of the patients, the natural healing processes may become effective sooner and terminate the rheumatic infection more promptly. Whether in this way or by some as yet unknown action corticotropin and cortisone minimize structural damage to the heart and thus reduce the incidence or severity of chronic heart disease cannot be answered at present.

SUMMARY

The results obtained with corticotropin and cortisone in 18 patients with severe rheumatic carditis are described. In all cases the clinical and laboratory signs of active carditis were unequivocal. The administration of corticotropin and cortisone was followed by a definite improvement in the general condition of all the patients. Fever decreased, "toxicity" disappeared, and joint manifestations subsided. This therapeutic effect was most striking in acutely ill patients.

Twelve patients were treated during their first rheumatic attack at varying intervals after the onset. Eight received a single course of therapy one to seven weeks following the first appearance of rheumatic manifestations. Active carditis subsided during treatment in four of these eight children, but in the other four clinical evidence of rheumatic activity persisted for six to nine weeks after cessation of therapy. The remaining four of these 12 patients were treated several months after onset. Three received two courses of therapy. However, carditis did not subside until five to seven weeks after the end of the second course. In the fourth child the rheumatic process was still considered to be active after three courses. Observations made two to nine months after complete cessation of therapy showed that all 12 patients had murmurs indicative of organic heart disease. Cardiac enlargement was definite in all but one case.

Six patients with antecedent rheumatic heart disease were treated during recurrent attacks. Therapy was instituted at intervals varying from 1 to 38 weeks from onset. In two patients, signs of activity disappeared within three weeks after therapy was begun, but relapse occurred in both within 10 days after the hormones were withdrawn. In two patients, active carditis persisted for 9 and 16 weeks, respectively, and in two patients for longer than 16 weeks. Signs of hyperadrenalism were observed frequently but in every instance disappeared gradually after cessation of therapy.

In this group of patients it was not clear whether the use of corticotropin or cortisone significantly decreased the duration of active carditis or influenced cardiac damage. Further studies with a greater number of patients and prolonged periods of observations are necessary.

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EOSINOPHIL LEVELS AS AN INDEX OF ADRENAL RESPONSIVENESS

FACTORS THAT AFFECT VALUE OF EOSINOPHIL COUNTS

C. D. Bonner, M.D., Boston

Since its first recognition as a separate morphological entity in 1865 by Max Schultze, the eosinophil cell has been the subject of much investigation. Earlier workers sought to clarify its morphology and function. By 1888 observers were studying differential counts, and in the same year Mayet described his eosin-glycerin method. In the next few years methods requiring the use of a counting chamber were devised by many authors quoted by Rud,[1] but none was successful; these methods were superseded by Dunger's method in 1910, which met with competition from exponents of the smear technique.[1]

The most exhaustive study in the field was done in Sweden by Rud from 1939 to 1943 and published in 1946-1947.[1] Here not only were attempts made to evaluate the methods of doing differential counts, but a study was made on the variation of the eosinophil count during the day, week, and seasons; the influence of position change, fasting, menstruation, sex, age, and constitutional type was also observed. After studying 550 subjects Rud concluded that his chamber method, using as a diluent 0.1 cc. of 10% magdala red, 6 cc. of acetone, 14 to 20 drops of 10% sodium carbonate solution, and 45 cc. of water, was superior to the smear method and that the eosinophil counts were reproducible, within a normal range, in the same subject from day to day and season to season, regardless of body position, menstruation, sex, age, and constitutional type. However, in many instances a drop occurred in the forenoon, with a rise later in the afternoon and night. This diurnal cycle was independent of food intake, but in a significant number of cases fasting caused the number of eosinophils to drop.

In the past few years attention has been focused anew on eosinophil counts and their relation to adrenal function. Thorn and his co-workers [2] devised a test for adrenal responsiveness which in effect is a measure of eosinophil levels before and after a stimulating dose of corticotropin (ACTH), and many investigators using corticotropin and cortisone have adopted this test. Recently Fisher and Fisher [3] studied eosinophil counts in normal subjects and found wide variations. They felt that this indicated that "it would be difficult to use this phenomenon as a sensitive indicator of pathologic variations." Because "Thorn's test" is done in the morning and forenoon hours on a fasting subject and because some investigators still use the smear method on finger or oxalated venous blood, it was felt that the question should be reevaluated.

METHODS

Two methods of determining the number of eosinophils were used.

1. In the chamber method a diluting fluid composed of equal parts of 0.1% phloxine and 0.1% methylene blue in propylene glycol was used.[3] Blood from a finger puncture was drawn into

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Mrs. Betsy Bundy, Miss Miriam Gobstoob, and Miss Vivian Freeman gave technical assistance in this study.

From the Clinical Research Laboratories of the Jewish Memorial Hospital and the Department of Medicine, Tufts College Medical School.

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2. Thorn, G. W.; Forsham, P. H.; Prunty, F. T. G., and Hills, A. C.: A Test for Adrenal Cortical Insufficiency: The Response to Adrenocorticotropic Hormone, J. A. M. A. **137**: 1005 (July 17) 1948.

3. Fisher, B., and Fisher, E. R.: Observations on the Eosinophil Count in Man: A Proposed Test of Adrenal Cortical Function, Am. J. M. Sc. **221**: 121, 1951.

a standard white blood cell count pipet in the usual manner, using the fluid as a diluent. The pipet was shaken by hand for two minutes, and then four counting chambers were charged. The chambers were allowed to stand for 15 minutes, and then the eosinophils seen in the nine squares of each chamber were counted and averaged. The figure obtained was multiplied by the factor 22.2 to obtain the final eosinophil count. If the number in one chamber varied greatly from the results in the other three, this figure was not used in calculating the average.

2. A blood smear from a finger puncture was made on a glass slide and stained with Wright's stain. A white blood cell count was also done on the blood from the same puncture or on oxalated venous blood. Eight hundred white blood cells in two groups of 400 were counted and the number of eosinophils noted. Then the number of eosinophils per 100 cells was computed and multiplied by the average of four white blood cell chamber counts expressed in units of 100. The result gave the absolute figure of circulating eosinophils. If the distribution of eosinophils in either group of 400 cells was uneven, then an additional 400 or a total of 1,200 cells were counted and the eosinophils per 100 cells calculated accordingly.

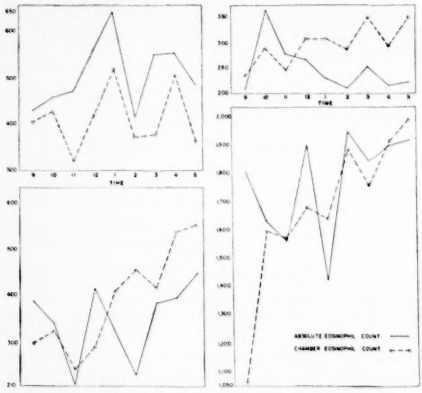

Chart 1.—Chart showing discrepancies between results of counts by chamber and smear methods expressed in eosinophils per cubic millimeter when only 400 cells were counted on the smears and only two chambers counted in the direct method of Randolph. Absolute eosinophil count indicates results obtained by counting eosinophils on the dry blood smear. Chamber eosinophil count indicates results obtained by counting eosinophils directly in the counting chamber. The time is expressed in hours from 9 a. m. to 5 p. m.

A total of 1,852 eosinophil counts were done, each checked by three persons. Seventeen normal subjects and 33 patients with various diseases were included in this study (39 women and 11 men). The age span was from 19 to 79 years. Diagnoses for the 33 patients included generalized arteriosclerosis, cerebrovascular accident, rheumatoid arthritis, carcinomas of various types, myasthenia gravis, fractured hip, syringomyelia, Paget's disease, Parkinson's disease, seborrheic dermatitis, multiple sclerosis, and progressive muscular atrophy.

PLAN OF STUDY

All counts were done by both the chamber method and the smear method from the same sample of blood. In 52 instances counts were computed in stages, i. e., two chambers or a group of 400 cells on smear were first taken, the absolute eosinophil count was made, and then the count was expanded to include four chambers and a group of 800 cells on smear. The final answers in each group were compared with the results obtained by counting half as many cells. In 20 patients an eosinophil count was performed by the chamber method on oxalated venous blood and also on blood from a finger puncture done at the same time.

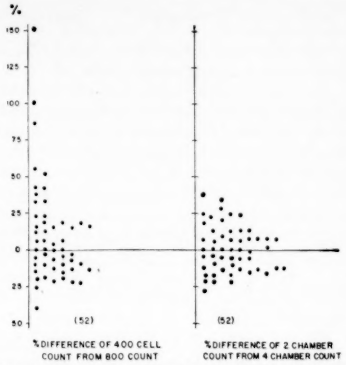

Chart 2.—Chart showing comparison of different results obtained by counting 400 cells or 800 cells on smears or by studying two chambers or four chambers using the direct method. Each dot represents one subject.

Forty-nine subjects who had been fasting since the previous evening were observed from 8 a. m. to 12 noon or from 9 a. m. to 1 p. m. Eosinophil counts were done either at 8 a. m. and 12 noon or at 9 a. m. and 1 p. m., the accepted hours for doing the Thorn test. A percentage drop in eosinophils of 50% or more has been considered a sign of intact adrenal function.

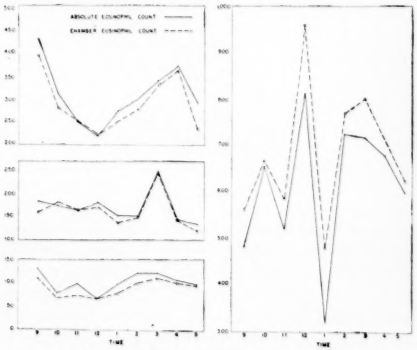

Chart 3.—Chart showing good correlation between chamber eosinophil counts and absolute eosinophil counts (obtained from blood smears) when 800 cells are counted on the smear, or when the eosinophils are counted directly in four chambers.

Fifty subjects (including the 49 who were observed while fasting) were allowed to eat according to their regular schedule, and eosinophil counts were again done at the same intervals. The same 49 subjects were again allowed to eat at their regular hours and the eosinophils were measured at 1 p. m. and 5 p. m.

One patient with rheumatoid arthritis who did not respond to corticotropin therapy but did respond to cortisone, one patient with panhypopituitarism, and four patients with Addison's disease were studied by hourly eosinophil counts throughout the day.

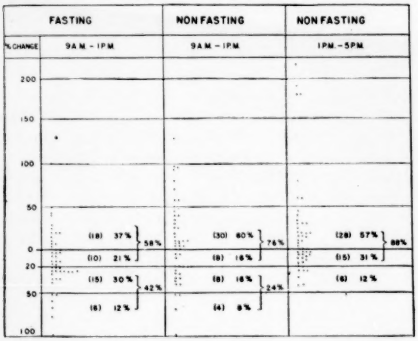

Chart 4.—Chart showing changes in eosinophil counts (by percentages of initial counts) occurring during fasting or normal food intake. The figures in parentheses represent the number of patients for each percentage. Each dot represents one subject.

One three subjects a Thorn test was done while they were fasting every Tuesday morning and while they were consuming food every Friday afternoon for four weeks in order to determine the reproducibility of the eosinophil response to 25 mg. of corticotropin (Armour) in the same subject.

RESULTS

1. In comparing the chamber method with the smear method it soon became obvious that if only two chambers were counted and only 400 cells were included in the

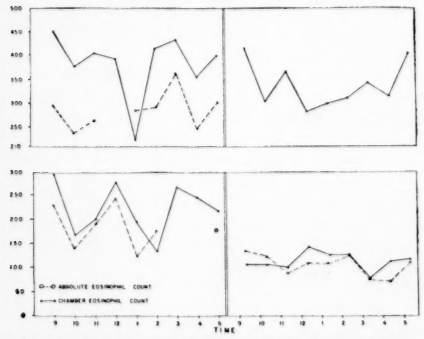

Chart 5.—Chart showing the fluctuation of eosinophils per cubic millimeter in four patients with Addison's disease with counts done hourly from 9 a. m. to 5 p. m. Absolute eosinophil count refers to counts done using the smear method, and chamber eosinophil count refers to the direct counting of the eosinophils in the counting chamber.

smear method, the results were not consistent. Chart 1 shows the results when counts were done every hour by both methods. The inconsistency is shown more pointedly in Chart 2, which gives the results when each count was done in two stages, counting first two chambers and 400 cells on each smear and then comparing the results obtained with those from the counts of four chambers and 800 cells on smears.

The 400-cell preliminary smear counts vary from —40% to +150% from the final 800-cell counts, while the two-chamber counts vary from —27% to +29% from the final four-chamber counts. Thus at the first stage the chamber count is more reliable than the smear count. However, when four chambers and 800 cells were counted, the two methods paralleled each other quite well (Chart 3). This was confirmed in many isolated counts done by both methods. Of 50 curves of results of counts done hourly during the day, 61% showed absolute counts by the smear method which were higher than the corresponding chamber counts. In 640 isolated counts 65% of the counts done by the smear method were higher than the chamber counts. The higher the eosinophil count, the greater was the possibility of a wider numerical difference. Except in rare instances, however, either type of count would have been adequate for clinical purposes.

Comparison of Repeated Tests in Same Subjects at Different Times of Different Days During Fasting or When Eating *

Fasting 9 A. M.–1 P. M.	Nonfasting 1 P. M.–5 P. M.
Cancer of Thyroid	
46.4	55.3
39.2	42.8
36.4	30.0
17.1	28.4
Cancer of Breast	
86.4	50.5
51.7	69.2
65.4	64.4
43.6	36.3
Normal Subject	
78.3	35.6
40.8	74.4
40.8	78.8
63.4	63.7

* The figures express decrease in eosinophils in percentages of pretest values.

2. When results obtained in freely flowing blood from finger punctures were compared with those obtained from oxalated venous blood, the finger blood gave higher results in 59% of the cases, while in 19% the results were identical. The variation between the results of counts seemed to be no different from that to be expected from the methodology in itself. Curves showing counts done every hour during the day were not identical when the counts were repeated on the same individual on different days, indicating that the daily pattern may vary widely.

3. It was found that 37% of the fasting subjects (Chart 4) had percentage changes of 0 and above, 21% had percentage changes between 0 and —20%, 30% had percentage changes of —20% to —50%, and 12% had changes below —50%. In this group of fasting patients 12% showed drops of the eosinophil counts, as if they had received corticotropin and had given a normal response to a Thorn test, and 30% of them had drops of from —20% to —50%.

4. In the group which ate at regular times and were tested from 9 a. m. to 1 p. m., 60% had percentage changes of 0 or above, 16% had falls between 0 to

—20%, 16% between —20% to —50%, and 8% had falls below —50%. Allowing the patients to eat resulted in a reduction of the number of those whose eosinophil counts decreased spontaneously.

5. When the same patients ate on their regular schedule and were tested from 1 p. m. to 5 p. m., 57% had percentage changes of 0 and above, 31% between 0 and —20%, 12% between —20% and —50%, and none of more than 50%. It is noteworthy that in none of these subjects did the number of eosinophils fall by a percentage that would simulate a normal response to corticotropin, and only six patients had falls between —20% to —50%. Three of these six had percentage changes of —22%.

6. The patient with rheumatoid arthritis who responded to cortisone and not to corticotropin showed a constant eosinophil level throughout the day. One patient with panhypopituitarism also showed little diurnal change of the eosinophil levels. Three of the four patients with Addison's disease, however, showed diurnal curves that fluctuated in the same manner as those of the other subjects, including normal subjects (Chart 5).

7. The results of this study of repeated Thorn tests with the Chamber method are summarized in the accompanying table. It can be seen that an individual occasionally responds differently at different times when a Thorn test is done, and may sometimes fall from the "responsive" into the "nonresponsive" range or vice versa. It would therefore seem that a nonresponsive test should not be regarded as conclusive until it has been repeated with the same results.

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COMMENT AND SUMMARY

From this study it appears that either the chamber count or the smear method for the counting of eosinophils may be used equally well for clinical purposes. The two methods parallel each other, provided that four chambers are counted and averaged or 800 cells are counted on the smear. The choice of method depends on the local circumstances. In a laboratory where many eosinophil counts are done by the same personnel, the chamber method is probably preferable because it is more rapid. A technician will develop the proficiency required for good results with this method. For those who do only occasional eosinophil counts it is perhaps advisable to use the smear method, because most technicians are experienced in the preparation of blood smears and in doing differential white blood cell counts. The results obtained from freely flowing finger blood or from oxalated venous blood do not differ significantly, but either one or the other should be used consistently.

Because it has been shown that fasting alone will cause a drop in number of circulating eosinophils, and since it has also been demonstrated that even in nonfasting subjects eosinophils drop fairly consistently in the forenoon and rise later in the afternoon, it is felt that the Thorn test may be more sensitive as an index of adrenal responsiveness if done on a nonfasting patient from 1 p. m. to 5 p. m. This has been true in my own, still limited, experience with 30 such tests in the afternoon.

It is interesting to note that in patients with Addison's disease daily curves of the number of eosinophils resembled those obtained in the group without adrenal disease. This contrasted with what might have been expected from the flat curves obtained in a patient with panhypopituitarism and in a patient with rheumatoid arthritis who did not respond to corticotropin. It suggests either that patients with Addison's disease have adrenal remnants still capable of being stimulated by certain stresses [4] or that mechanisms exist for the control of eosinophil levels other than cortisone-like substances. Such mechanisms might also account in part for the fact that the same subject will respond differently to the same stimulating dose of corticotropin at different times in respect to the level of the circulating eosinophils.

30 Bennet St.

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THE SULFONAMIDES AND ANTIBIOTICS IN TRACHOMA

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The following preparations were used and the results observed in a series of over 3,500 patients with trachoma at the Missouri Trachoma Hospital during 1941-1951: sulfanilamide, sulfapyridine, sulfathiazole, sulfathiazine, sulfacetamide ("albucid"), sodium sulfacetamide ("albucid" soluble), sulfamylon* (4-amino-2-methyl benzene sulfonamide hydrochloride), diacetylaminoazotoluene (prontosil*), combisul* (a combination of sulfadiazine, sulfamerazine, and sulfathiazole), sulfisoxazole diethanolamine (gantrisin*), penicillin, bacitracin, streptomycin, chloramphenicol (chloromycetin*), aureomycin, and terramycin. Some of the sulfonamide drugs were used in tablet form for internal medication and others in aqueous solution, as drops for local instillation into the conjunctival sac. Both of these methods were usually combined, and an overnight coating of the sulfa ointment was also used. The antibiotics were prepared in fresh, buffered, aqueous solutions daily, from crystalline powders supplied in sterile vials, and used for topical application every two hours. Only surface applications of antibiotics were used, since it was felt that systemic injections of adequate dosage do not produce measurable concentrations in the ocular, and particularly the conjunctival, tissues and fluids. Moreover, it was felt that, in trachoma at least, subconjunctival injections of antibiotics were not justifiable, since simpler methods appeared as effective.

Medical Director, Missouri Trachoma Hospital.

Read before the Section on Ophthalmology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

THE SULFONAMIDES

All the sulfonamides named in this report were found to be beneficial in trachoma. Their action was generally mild, or bland, on the conjunctiva. Some sulfonamides, such as sulfanilamide, diacetylaminoazotoluene, sulfacetamide, and sodium sulfacetamide, caused toxicity; others were not highly soluble and afforded little concentration of solid when in solution. For these reasons, the early sulfonamides (previous to 1945) were discarded in favor of the more recent, highly soluble drugs, such as gantrisin,* sodium sulfacetamide, sulfadiazine, and combisul.* Since 1945, these products have been found to be the most effective and least toxic of the available sulfonamides.

Sodium sulfacetamide forms a stable, highly soluble, aqueous ophthalmic solution and, if used in no higher than a 10% concentration, is effective in trachoma with only occasional toxic side reaction. Stronger solutions are ineffective because of irritation. Gantrisin* is a newer, highly soluble, well-buffered, aqueous ophthalmic solution and is the ideal sulfonamide in trachoma because of its minimal toxicity, blandness of action, and therapeutic effectivity. It is used in 4.3% solution (optimal for local use), and as a tablet of 7.7 grains (0.5 gm.) for internal use. Neither tablet nor solution is toxic. Combisul,* consisting of equal parts by weight of sulfadiazine, sulfamerazine, and sulfathiazole, is very effective in trachoma when used as tablets of 0.5 gm. for internal medication. Its toxicity is minimal, and it requires no alkalinization for use. Sulfamylon* hydrochloride, 1% solution, is a well-buffered, aqueous, aromatic ophthalmic solution but was not found to be so effective or so bland as gantrisin,* 4%, and sodium sulfacetamide, 10%. Sodium sulfacetamide, 10% ointment, and gantrisin,* 10% ophthalmic ointment, form stable emollients for coating the conjunctiva during the night. Treatment at Missouri Trachoma Hospital was a three-way attack: (1) local instillation every two hours of gantrisin,* 4.3% solution, daily, for from 10 days to 3 weeks (occasionally, sodium sulfacetamide, 10% solution, was used instead); (2) internal medication with gantrisin* given orally in four divided daily doses, according to age and weight for the first seven days; and (3) coating the conjunctival surfaces nightly with gantrisin,* 10% ophthalmic ointment or sodium sulfacetamide during the entire period of treatment.

Early subsidence of all inflammatory symptoms, gradual resolution of pannus if incipient, and the rapid disappearance of photophobia and blepharospasm resulted. Mild entropion and trichiasis showed improvement by unfolding of the beginning incurvation of lids. Advanced cicatricial entropion does not improve. Early pannus formations were fairly well resolved. Moderately advanced vascularizations did not resolve. Ulcerations improved as far as the general condition improved. Opacification was not affected, except as the general inflammatory condition subsided. Cicatrization, once established, was not affected. Early entropion that was of blepharospastic nature improved only after sulfonamide treatment.

THE ANTIBIOTICS

Penicillin, bacitracin, streptomycin, chloramphenicol, aureomycin, and terramycin, in this order, were used during the past five years at the Missouri Trachoma Hospital, but with disappointing results, as a specific cure for trachoma. The antibiotics have no effect on trachoma per se, but, for clearing up secondary infections associated with trachoma, they are excellent.

Cases of trachoma with concomitant blepharitis, purulent blennorrheas, pneumococcic ulcers, or staphylococcic infections of the tear sac responded quickly and well to irrigations with penicillin, terramycin, aureomycin, and chloramphenicol, and excellent results were also obtained in these infections with ointments of bacitracin, penicillin, and terramycin. However, no direct effect upon the underlying trachomatous condition itself was observed to follow with antibiotics. Trachoma patients treated with antibiotic solutions and ointments every day for several weeks and longer failed to show any improvement in clearing of incipient pannus, relief from turgescence of the retrotarsal fold, resolution of granules, or even from the increased lacrimation and itching that is almost always present in all trachoma. When secondary infections complicated trachoma, antibiotics relieved the symptoms to some degree and produced a partial subsidence of inflammation. Very purulent secretions cleared remarkably within a few days after treatment. In such cases, the underlying trachoma seemed improved, but this was only because superimposed infection was alleviated and controlled by application of antibiotic solutions or ointments.

COMMENT

There has been much discussion during the past decade as to whether the sulfonamides and the antibiotics have a specific effect on the virus in trachoma. The majority of investigators claim the sulfonamides do have a specific effect. Thygeson, Sorsby, Wilson, Bietti, Richards, Forster, Poleff, Freyche, Loe, and Cosgrove believe they do. Thygeson states that, in cases in which specific inclusion bodies were found previous to administration of sulfonamides, they could not be found after treatment with this drug. Others have demonstrated that Prowazek inclusion bodies disappear from the conjunctiva in a few days or more following sulfonamide treatment. Sorsby concludes from his observations that the sulfonamides are specific against the virus of trachoma and not merely against any associated secondary infections. I believe that further bacteriologic research will conclusively prove specificity of sulfonamides for the virus of trachoma.

The antibiotics, too, are at present under fire regarding their specificity in trachoma. Many foreign observers and some in America believe them to be specific. Some workers, however, draw conclusions too soon, before they have properly evaluated the type of infection and the time and number of cases under study. A long time must elapse and a large number of cases must be studied before it is possible to decide whether any agent is the

specific drug for trachoma. I do not believe that trachoma per se is affected materially by aureomycin or any other antibiotic used in this work. I think some foreign observers are led to believe that antibiotics are beneficial because of the existence of florid secondary infections almost always attending trachoma in the Near East and Orient. In Egypt, for instance, trachoma is almost always secondarily infected with pneumococci, gonococci, or Koch-Weeks infection, and often trachoma is preceded by one of these conditions. Since antibiotics are effective generally against these infections, a rapid improvement of the over-all clinical picture results, and the credit is given essentially to trachomacidal action. It would not be too difficult to draw premature conclusions regarding specificity for aureomycin and other antibiotics. In the Missouri Ozarks region, trachoma infection is usually unattended with secondary infections; thus, antibiotics have had their opportunity to prove themselves, if effective, in cases of pure trachoma, but have failed. In the Orient, on the other hand, because of the many, consistent, almost constant, secondary and mixed infections present with trachoma, the antibiotics have had a better chance to show dramatic effects and give an impression of cure. Not until antibiotics can relieve primary, uncomplicated trachoma infection, with inflammation, turgescence, incipient pannus, and photophobia, or can be proved bacteriologically to have a direct viricidal action, will it be possible to draw accurate conclusions in this matter.

CONCLUSIONS

1. The primary role of the sulfonamides in the treatment of trachoma is established. They stand as first therapeutic choice because of their relative mildness of action and apparent specificity against the trachoma virus.

2. Antibiotics are of secondary help in clearing the common pus-producing organisms attendant to trachoma, and thus serve to shorten the total morbidity period of this disease.

3. Although therapeutic agents that give speedier effects and possess greater flexibility would be desirable, to date the sulfonamides stand superior to all other therapeutic agents used thus far in this ocular disease.

Collagen Diseases and Cortisone.—The two syndromes—rheumatoid arthritis and rheumatic fever—are not far separated in their nature and in their response to cortisone. Similar comparisons hold for some of the other collagen diseases. Perhaps the most hopeful aspect of the study is the wide portion of clinical medicine which is influenced by this hormone. The unexpected and far-reaching influence of cortisone on many diseases may be produced through its control of some causative agent which is common to all of them. The nature of this agent is unknown, but I agree . . . that the hypothesis of the adaptation syndrome of Selye . . . is not acceptable. Today it can be said that cortisone will relieve the pain and symptoms of rheumatoid arthritis, and it constitutes a life-saving measure for other syndromes, but to the clinician interested in research it will be a key which will unlock the doors of barriers and reveal secrets long hidden. —Edward C. Kendall, Ph.D., The Adrenal Cortex and Rheumatoid Arthritis, *British Medical Journal*, Dec. 1, 1951.

CLINICAL NOTES

PROPYLTHIOURACIL-INDUCED AGRANULOCYTOSIS, TOXIC HEPATITIS, AND DEATH

REPORT OF A CASE

Arthur R. Colwell Jr., M.D.
Don E. Sando, M.D.
and
Samuel J. Lang, M.D., Evanston, Ill.

Because of its therapeutic effect and minimal toxicity, propylthiouracil has become the drug of choice in the treatment of hyperthyroidism. Leukopenia developed in only 10 of 672 patients who received the drug in preparation for thyroidectomy.[1] Recently, however, administration of propylthiouracil has been reported to cause death or severe disability in a few cases. Livingston and Livingston [2] reported a nonfatal case of toxic hepatitis following treatment with the drug. Two other fatalities from agranulocytosis have been described previously in the literature.[3] This is a report of a third death due to agranulocytosis, associated with early toxic hepatitis, following the administration of propylthiouracil.

REPORT OF CASE

History.—A white woman, a secretary, aged 60, was admitted to Evanston Hospital on Aug. 17, 1950. Until two weeks before admission she had been perfectly well. At that time she noticed palpitation and a "tightness" in the chest on reclining or following exertion. A week later she had shortness of breath on walking to work in the morning, followed by ankle edema in the evening. There was an occasional nonproductive cough, but no orthopnea nor paroxysmal nocturnal dyspnea. The patient had also noticed nervousness, irritability, and a slight tremor of the hands in the two weeks prior to admission. The past and family history were noncontributory, and history by systems disclosed no abnormalities.

Physical Examination.—The patient was a nervous, pale, somewhat undernourished woman, with an anxious expression. The oral temperature was 99 F, the pulse rate 120, and the blood pressure 150/70 mm. Hg. The skin was warm and moist. There was no exophthalmos nor lid lag. The fundi were normal. The teeth were in poor condition. No mass was palpable in the region of the thyroid gland. Crackling rales were present at both lung bases. There was a sinus tachycardia, which was not changed by rest nor exercise; the heart was not enlarged, and the sounds were normal. The liver was not palpable. There was 1+ pitting ankle edema.

Hospital Course.—The clinical impression was that the patient had arteriosclerotic heart disease with congestive failure. She was digitalized with 1.2 mg. of digitoxin, given in divided doses. This had no effect on the tachycardia, and digitoxin was discontinued on the third day because of nausea and vomiting. A low-sodium diet, 0.2 gm. of aminophylline three times daily, and 1 gm. of ammonium chloride five times daily were also administered. On the second hospital day, 0.2 gm. of quinidine sulfate

From the Department of Medicine, Evanston Hospital.

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was administered three times daily because of a transient episode of auricular fibrillation. The heart size was normal on a roentgenogram, and an electrocardiogram indicated only tachycardia and digitalis effect. Because of the lack of response to digitalis, hyperthyroidism was suspected. The blood cholesterol level was 149 mg. per 100 cc., the basal metabolic rate was +40%. Propylthiouracil therapy, 300 mg. given daily in three doses, was instituted on Sept. 1, and potassium iodide, 5 minims (0.308 cc.) daily, on Sept. 7. The pulse rate continued to vary between 100 and 110. A second trial with digitoxin only produced further nausea and vomiting without slowing the pulse rate. By Sept. 5 the blood cholesterol had risen to 222 mg. per 100 cc., and the basal metabolic rate was +6%. The hemoglobin value was 11 gm. (71%), red blood cell count 3,620,000, and repeated white blood cell counts from Sept. 5 to Sept. 15 varied between 3,500 and 5,000. On x-ray examination, the gallbladder, esophagus, stomach, duodenum, and colon were normal. There was no evidence of a substernal thyroid. The patient was discharged on Sept. 19, somewhat improved, with instructions to take 300 mg. of propylthiouracil daily. A white blood cell count reported after discharge was 2,550 cells.

Readmission.—On Oct. 2, 13 days after discharge, the patient was readmitted to the hospital. She had undertaken a 100-mile motor trip one week after discharge. While she was away, malaise, fever, chills, anorexia, and a nonproductive cough had developed. All medication had been voluntarily discontinued on Sept. 29. On readmission, the oral temperature was 103.2 F, pulse rate 120 and irregular, respiration rate 20, and blood pressure 80/40 mm. Hg. First and second degree burns from locally applied heat were present on the abdomen and chest. A few dry rales were heard in the left lung base. There were alternating periods of auricular fibrillation and flutter. The red blood cell count was 2,900,000; the white blood cell count was 250. Treatment with 100,000 units of penicillin every three hours, morphine sulfate, intravenous fluids, quinidine, and blood transfusions was instituted.

Laboratory findings the day after admission (following two transfusions) were as follows: hemoglobin, 11.5 gm. (74%); red blood cells, 3,500,000; white blood cells, 2,380; polymorphonuclear leukocytes, 7; lymphocytes, 47; monocytes, 45; basophil, 1; and thrombocytes, 64,000. The blood contained nonprotein nitrogen, 55.7 mg. per 100 cc.; total cholesterol, 216 mg.; cholesterol esters, 104 mg.; total serum proteins, 4.8 gm.; albumin, 3.1 gm.; globulin, 1.7 gm.; and total serum bilirubin, 10.9 mg. The thymol turbidity was 2.6 units, cephalin flocculation, 4+, and alkaline phosphatase, 1.7 Bodansky units. The urine showed 4+ albuminuria.

The day after readmission, the patient became clinically jaundiced. She complained of anorexia, dyspnea, nausea, mild cramping pains in the lower abdomen, and diarrhea with watery, greenish stools. The temperature remained at 102 F orally. An electrocardiogram showed auricular fibrillation, but on the following day the rhythm was normal. By auscultation, it was felt that there were intermittent periods of auricular fibrillation, auricular flutter, and regular sinus rhythm. The white blood cell count dropped to 1,200 and then to 700, with 4 polymorphonuclear leukocytes, 66 lymphocytes, and 30 monocytes. The red blood cell count was 3,490,000, with a hemoglobin level of 10.5 gm. per 100 cc. (68%) and 64,000 thrombocytes. The chest was normal on x-ray examination, but clinically there appeared to be pneumonia of both lower lobes. The patient died on Oct. 5, 1950. The clinical impression was that the patient had aplastic anemia and leukopenia due to propylthiouracil, upper respiratory infection with possible bronchopneumonia, and organic heart disease due to hyperthyroidism, with auricular fibrillation and flutter.

Autopsy.—The body was that of a well-developed, fairly well-nourished, white woman of 60 years, measuring 161 cm. in length and weighing an estimated 55 kg. The scleras and skin were markedly icteric, and there was slight pitting edema of both lower extremities. All serous surfaces were smooth, glistening, and yellowish.

The heart was moderately hypertrophied (330 gm. in weight) and there were minimal arteriosclerotic changes in the coronary arteries. The lungs were subcrepitant, and scattered throughout the parenchyma were small, deep maroon, nodular areas. A moderate amount of frothy, yellow fluid could be expressed from the bronchioles. Sections of the lungs showed bronchopneumonia, characterized by early necrosis of the bronchioles, surrounded by alveoli filled with red blood cells, lymphocytes, and bacteria. No polymorphonuclear cells were found. The presence of pigment-containing macrophages indicated chronic pulmonary congestion.

The liver weighed 1,620 gm. and had a normal brown color. Other than having a moderate "nutmeg" appearance, the sectioned surface appeared normal. Microscopically, there was a fairly marked loss of liver cord cells around the central veins but no evidence of focal areas of necrosis elsewhere, or of biliary stasis. There was a moderate degree of fatty metamorphosis, and a few lymphocytes were seen in the periportal areas. These changes suggested early toxic hepatitis. The extrahepatic biliary tree was patent, and there were no lesions of the gallbladder. The spleen weighed 290 gm. The parenchyma was brown-red and friable, with a decrease in corpuscular markings. With the exception of a congenital double pelvis and double ureter on the left, the kidneys showed no lesions.

The appendix, which was lying medially and loosely adherent to the omentum, was edematous and reddened. The serosal surface was roughened, and several purple hemorrhagic bands encircled the organ. Yellow-white coalescing patches surrounded by bright red hemorrhage covered the mucosal surface. There was a similar, though not so pronounced, appearance of the intestinal mucosa from the transverse colon through the rectum. These lesions in no place perforated the wall. Microscopically, all layers of the appendiceal wall showed marked hemorrhage, lymphocytic infiltration, and necrosis (severest in the mucosa and submucosa). The lesions in the colon closely resembled those in the appendix; however, the muscular wall was only slightly involved. In both organs, there were numerous bacillary organisms and no polymorphonuclear leukocytes. These changes represented acute ulcerative appendicitis and colitis, which probably appeared terminally following the development of the agranulocytosis.

The bone marrow showed a decrease, though not an absence, of the cells of the granulocytic series, and only an occasional adult form was seen. Erythropoiesis was active. The thyroid gland weighed 38 gm. and appeared grossly normal. On microscopic section, the gland showed marked epithelial hyperplasia, characterized by numerous papillary infoldings into the acini, and reduction of colloid. This appearance might have been caused by treatment with propylthiouracil or by an increased secretion of thyroid hormone.

COMMENT

In our opinion, death in this case was due to acute fulminating septicemia secondary to agranulocytosis, which resulted from toxic suppression of the bone marrow by propylthiouracil. Contributing to the septicemia were the acute ulcerative appendicitis and colitis, as well as the pneumonia, which resulted from loss of the normal defense mechanisms against infection, attendant with agranulocytosis. Whether the hepatitis was caused by propylthiouracil administration, by a virus infection contracted before admission to the hospital, or by the terminal septicemia is difficult to determine, but the first possibility seems most likely. Recovery from the hepatocellular jaundice similar to that in Livingston's case [2] might have occurred, if infection from other sources had not appeared and caused death. In our case the toxic effects of propylthiouracil were irreversible, in spite of the fact that the drug had been discontinued a week before death.

In addition to the case of agranulocytosis and jaundice from propylthiouracil previously mentioned,[2] several cases of toxic hepatitis due to thiouracil poisoning have

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been reported.[4] Of these cases, histological studies were possible in only two. Gargill and his co-workers, [4b] in a section taken by biopsy 18 days after the onset of jaundice, found distention of the bile canaliculi and small bile thrombi, indicating acute biliary stasis. In an autopsy specimen taken 59 days after the onset of jaundice, Holoubek [4c] described focal and central necrosis, as well as plugging of the bile canaliculi.

The histological findings in the liver of our patient were not remarkable. The loss of liver cord cells around the central veins was more marked than would be expected from chronic passive congestion and probably represented an early stage of toxic hepatitis. The minor degree of this change may be explained by the apparently short duration of hepatitis before death occurred.

SUMMARY

A third case of death from agranulocytosis due to propylthiouracil therapy is described. There was accompanying toxic hepatitis, apparently resulting from administration of proplythiouracil.

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4. (*a*) Footnote 3b. (*b*) Gargill, S. L., and Lesses, M. F.: Toxic Reactions to Thiouracil: Report of Cases with One Fatality, J. A. M. A. **127**: 890-898 (April 7) 1945. (*c*) Holoubek, J. E.; Mathews, W. R., and Hollis, W. J.: Thiouracil Hepatitis, Am. J. Med. **5**: 138-142 (July) 1948. (*d*) Moore, F. D.: Toxic Manifestations of Thiouracil Therapy, J. A. M. A. **130**: 315-319 (Feb. 9) 1946.

COARCTATION OF AORTA WITH SURGICAL CORRECTION AT AGE FORTY

REPORT OF A CASE

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As a consequence of the demonstration by Crafoord,[1] Blalock,[2] and Gross [3] that coarctation of the aorta in man is amenable to surgical cure, there is an increased interest and incentive in the diagnosis of what has previously been an incurable clinical curiosity. Gross [4] has reported the results in 100 such patients operated on by him. Of these 11 did not survive and 9 had only exploratory operations. Of the remaining 80, 71 were cured completely, 8 obtained satisfactory relief, and 1 had no relief.

There has been some question about operating on older people for the correction of coarctation of the aorta. Gross considered that the optimal age for performance of the procedure was between 6 and 20 years. He felt that in persons older than 25 the aorta was too arteriosclerotic for manipulation and suture. Clagett [5] successfully performed a Blalock procedure on a 34-year-old man, the oldest patient with coarctation to have been operated on up to that time. In his discussion he stressed the disadvantages of operating on a patient that old because "there are rather severe arteriosclerotic changes in vessels of persons who have had coarctation for a long period." Gross [6] as late as 1949 mentioned that "some excellent results have been obtained in patients in the late twenties." His oldest patient up to that time had been 30 years old. In his later publication [4] age is not mentioned. Blalock, in discussing Gross' [6] paper, reported a successful operation in a man aged 41. He believed this patient was the oldest ever operated on for coarctation.

The purpose of this particular paper is to describe a patient with coarctation of the aorta successfully operated on at the age of 40. This patient presumably is the second one over the age of 40 to have had this operation.

REPORT OF A CASE

J. P., a white automobile plant superintendent, first learned that he had hypertension six years prior to this hospital admission. One year later a thymectomy was done at another hospital. In spite of the hypertension, he remained relatively asymptomatic until three months prior to admission, when he began to notice gradually increasing palpitation, sweats, and flushing of the face. There was a 15 lb. (6.8 kg.) weight loss. On questioning, the patient said that his feet had been cold for a number of years. The past history and family history were not relevant.

Examination revealed a well-developed, well-nourished adult with flushed facies, who appeared apprehensive but not ill. Blood pressure in the left arm was 174/102 and in the right arm 178/90. The radial pulse rates were equal, and the brachial pulses were easily visible. The femoral pulse was weak and exhibited a slow rise. The popliteal and dorsalis pedis pulses could not be felt, and a blood pressure in the legs was unobtainable. Both lower extremities were colder than normal.

There were minimal changes in the retinal vessels, including a slight increase in the light reflex of the arterioles and moderate arteriovenous nicking. The visual acuity ratio was 2: 1. In the neck a few posterior cervical nodes and gross pulsations in both supraclavicular areas were noted.

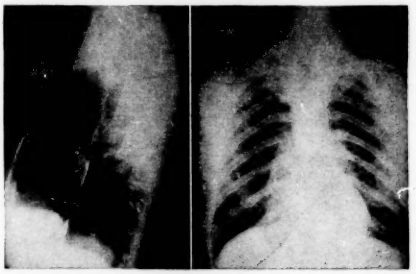

Fig. 1.—Roentgenograms showing the heart to be of normal size. The aortic knob is not visible. Multiple notching of the inferior borders of the ribs is present.

The left side of the thorax appeared more prominent than the right. On auscultation there was a loud systolic murmur that could be heard over the entire precordium. This murmur could be traced down along the right sternal border almost to the umbilicus and along the left sternal border to a point beyond the umbilicus. It could be heard, also, in the axillas and in the interscapular area. Pulsations could be felt in various areas of both the anterior and posterior chest fields, and in some of these areas they could be seen. No diastolic murmur was heard. The remainder of the physical examination disclosed no abnormalities.

The blood count showed 4,520,000 red blood cells and 7,800 white blood cells, with 66% segmented polymorphonuclear cells, 1% stab forms, 31% lymphocytes, 1% eosinophils, and 1%

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monocytes. The hemoglobin value was 85% (Sahli). The Kahn reaction was negative. The urine had a specific gravity of 1.018 and contained an occasional white blood cell. The urine contained no albumin, glucose, casts, or red blood cells.

A urine concentration test showed a range of specific gravity from 1.008 to 1.020. The phenolsulfonphthalein excretion rate was 30% in 15 minutes and 50% in one-half hour. Urea clearance was 196% in the first specimen and 220% in the second. The nonprotein nitrogen concentration was 31.0 mg. per 100 cc. Serum protein level was 7.18 mg. per 100 cc.

Oscillometric readings were as follows: right wrist, ½ unit; left wrist, ½ unit; right calf, 1½ units; left calf, 1 unit; right ankle, ¼ unit; and left ankle, ¼ unit.

A roentgenogram of the chest (Fig. 1) revealed normal lung fields and a normal-sized heart. The aortic knob prominence was absent. There was notching on the inferior margins of the ribs. An electrocardiogram was entirely normal.

On April 26, 1950, an operation was performed by Dr. Dewey Dodrill. A long parascapular incision was made on the left thorax, extending from about the level of the third thoracic vertebra midway between the spine and the vertebral border of the scapula downward, curving beneath the tip of the scapula and then anteriorly to reach the anterior axillary line. The musculature of the chest wall presented huge pulsating arteries, some as large as lead pencils, which had to be carefully isolated and

Fig. 2.—Two views of the excised segment of aorta. The lower view is looking into the lumen of the vessel, demonstrating that the aorta is completely occluded.

ligated with silk suture. The scapula was retracted, the fourth rib resected subperiosteally, and the pleural cavity entered.

When the lung was retracted downward and forward, the coarctation was found just distal to the left subclavian artery and was approximately 2 cm. in diameter. The left subclavian artery was almost 1 in. (2.5 cm.) in diameter; the pressure within it was very high. The adventitia of the aorta was incised, and then by blunt dissection the aorta was freed around the constricted area and from there proximally to a point beyond the origin of the left common carotid. Three sets of intercostal arteries had to be divided, all of which were hugely dilated. These entered the aorta just distal to the coarctation and carried blood from the collateral circulation to the lower thoracic aorta. It was noted that these collateral vessels were hard, rigid, and nonresilient, presumably because of atheromatous change. One of them was so friable that ligation was impossible, since the ligature cut right through its wall. This vessel was sewed with fine interrupted silk suture.

A modified Potts clamp was placed on the proximal portion of the aorta, which partially occluded the common carotid. This was unavoidable, since the subclavian and common carotid were very close together. A coarctation clamp was then placed on the distal aorta, after which the constricted area was resected. The ends of the aorta were approximated and sutured with 0000 arterial silk, with a continuous everting type of mattress suture which was interrupted at three points. No atheromatosis had been noted within the lumen of the aorta itself. The distal clamp on the aorta was then released, revealing two small bleeding points, which were controlled with interrupted silk sutures. The proximal clamp on the aorta was next released gradually over a period of five minutes. There was no precipitous fall in blood pressure as this latter clamp was released. The resected portion of the aorta was examined, and it was noted that its lumen was completely occluded.

During the operation the patient received 3,500 cc. of blood. His condition remained good throughout the procedure. The postoperative course was uneventful. On the day following surgery the blood pressure in the left arm was 148/118 and in the right arm 152/120, in the left leg 170/122 and in the right leg 168/124. The femoral pulses were increased, and the dorsalis pedis pulses were palpable for the first time. The precordial murmur gradually became fainter and finally disappeared. The sounds that had previously been heard over areas of collateral circulation (axillas, posterior chest, and abdomen) all disappeared. Oscillometric readings on the 20th postoperative day were as follows: right thigh, 4 units; right calf, 3½ units; right ankle, 1 unit; left thigh, 3 units; left calf, 1½ units; and left ankle, ¾ units. The color and temperature of the lower limbs had returned to normal. The patient was discharged from the hospital on the 19th postoperative day.

When last seen, on June 23, 1950, the patient was entirely asymptomatic and had returned to his former employment. The blood pressure was 140/80, the pulse rate 88 per minute, and the heart sounds normal. The lower extremities were entirely normal as to warmth, color, and freedom from symptoms. The pulses in the legs were full and adequate bilaterally.

SUMMARY

The factor of age with reference to the operability of coarctation of the aorta is discussed. Coarctation successfully corrected by surgery in a man 40 years of age is described. This is believed to be the second case on record in which a patient of 40 or over has had this operation with a successful outcome. It is noteworthy that in this patient, although the intercostal vessels were markedly sclerotic, the aorta itself was not atherosclerotic.

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RHINOSCLEROMA SUCCESSFULLY TREATED WITH STREPTOMYCIN

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Rhinoscleroma is not a common disease in the United States, but its study is of interest, since it is a serious progressive infection of disputed etiology.

Rhinoscleroma is widespread throughout Europe,[1] Asia,[1b] and Hawaii.[2] The condition is said to be commonest in Central America.[3] In the United States and Canada 102 cases had been reported by 1942; only 16 of the patients were native born.[4]

Rhinoscleroma begins as a nasal catarrh, sometimes with a foul odor, and gradually progresses to a stage

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characterized by cartilage-like nodules that tend to occlude the nasal passages. Since Frisch [5] in 1882 described an encapsulated gram-negative rod as the main cause of rhinoscleroma, there has been much discussion as to the actual significance of the organism. It has been impossible to fulfil Koch's postulates because the Frisch bacillus (now called Klebsiella rhinoscleromatis) has not produced rhinoscleroma when inoculated into experimental animals [6]; likewise, attempts to produce the disease in human volunteers have been unsuccessful.[7] Such studies, together with the fact that K. rhinoscleromatis has been recovered from well persons,[8] have led to the postulation that a virus may be the true causative agent of rhinoscleroma

Our case is similar to another in which treatment was given the same year (1946), reported by New and others [8]; they reported an encouraging response to streptomycin therapy. Since that time five cases have been reported in the United States in which there was response to streptomycin or dihydrostreptomycin therapy.[9] Also, three patients in Yugoslavia [10] and one in France [11] have favorably responded to this antibiotic.

It has been possible to follow our patient for three years after initial treatment, thus affirming that arrest of the disease was apparently accomplished, not temporary remission. All the cases in which treatment was with streptomycin, since there was response to this therapy, give support to the belief that the Frisch bacillus is the etiological agent of the disease because the Frisch bacillus is a gram-negative rod showing in vitro sensitivity to streptomycin.

REPORT OF A CASE

A Latin American woman, 27, came to the office Aug. 27, 1946, with a complaint of nasal obstruction and severe sore throat. The patient had lived in south Texas all her life and had never visited Mexico. About two or three months previously she had noticed some difficulty in her nasal breathing, which was soon followed by a sore throat.

Examination revealed that the anterior nares were partially obtructed with granulomatous tissue. The soft palate was markedly inflamed. This patient was seen on several occasions and finally consented to enter the hospital on Dec. 11, 1946. At this time the nose was completely occluded with granulomatous tissue. There was a destructive lesion of the soft palate with complete loss of the uvula. Numerous sections were removed from both nostrils as well as from the soft palate and sent to the laboratory.

Pathologist's Report.—The specimen consisted of several pieces of tissue removed from within the nasal cavity. These varied considerably in size and shape. Each tissue had one border covered or partially covered by stratified squamous epithelium. This was somewhat atrophic with complete absence of the rete pegs. The stratum mucosum, including the basal cell layer, was uniform in structure. In the outer portion of the corium were many Mikulicz cells. These were large cells with small nuclei and foamy cytoplasm. With proper staining, small gram-negative rods could be seen within these cells. Many broad bands of connective tissue were scattered throughout this granuloma, in some areas completely replacing the other cellular elements. The majority of cells in this granulomatous process were plasma cells. With these were some round and ovoid acidophilic structures called Russell bodies.

Russell bodies were found rather frequently in rhinoscleroma, and the presence of Mikulicz cells containing bacilli resembling those of the Frisch bacillus is diagnostic indication of the disease.

Bacteriologist's Report.—Acid fast smears for the leprosy bacillus were negative. Aerobic and anaerobic cultures showed abundant growth of a gram-negative rod having a highly mucoid colony. Tests for Neufeld's reaction with anti-Friedlander serums types A, B, and C were negative. This lack of quellung and negative mouse pathogenicity tests ruled out the organism as a member of the Friedlander group. Culturally and biochemically the isolated organism is compatible with K. rhinoscleromatis, as described in Bergey's manual (fifth edition). Antibiotic sensitivity tests on the isolated organism showed it to be resistant to 10 whole units of penicillin per cubic centimeter. It was completely inhibited by 5 units of streptomycin per cubic centimeter and partially inhibited by 1 unit per cubic centimeter.

There were no reports of streptomycin having been used up to this time for the treatment of rhinoscleroma, but in view of the sensitivity tests, this antibiotic was chosen for therapeutic trial.[12]

The patient reentered the hospital on March 15, 1947. She was given a total of 28 gm. of streptomycin in ¼ gm. doses every four hours. At the end of the fifth day the lesion in the soft palate had completely healed. Cultures from the nares as well as the soft palate were taken repeatedly and were negative. At the end of six months and again at the end of three years no evidence of the organism was found in either cultures or sections. The patient was last seen on Feb. 8, 1950. At this time the palate was completely healed, and both nostrils were free of granlomatous tissue. There was some constriction of both nares due to scar tissue but no evidence of a lesion.

COMMENT

In addition to the fact that rhinoscleroma responds to streptomycin therapy, there is another type of evidence which strongly supports the theory that rhinoscleroma is caused by the bacillus which bears its name. Complement fixing antibodies to this organism have been found in the majority of rhinoscleroma patients examined, and the complement fixation test is proving a practical method of diagnosing the condition.[13]

SUMMARY

A patient with rhinoscleroma treated with streptomycin showed clinical improvement within five days after the beginning of therapy, and cultures promptly became negative for Klebsiella rhinoscleromatis. Lesions did not recur during a subsequent three year period of observation. This dramatic response to streptomycin therapy in this patient and those mentioned elsewhere lends additional weight to other existing evidence that Klebsiella rhinoscleromatis is the causative agent in the disease from which it is named.

705 E. Houston St. (Dr. Russell).

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CONGENITAL ECTODERMAL DEFECT WITH AMASTIA

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Congenital ectodermal defect is a rare syndrome characterized by hypotrichosis, absence of sweat glands, absence of sebaceous glands, adontia or hypodontia, a characteristic facies, and, occasionally, absence of the mammary glands. About 80 such cases have been reported, but only 4 of these (all male) have had absence of the breasts and nipples.[1] The purpose of this report is to record a case of this variety.

A brief consideration of the clinical appearance of patients with ectodermal defect (Fig. 1) reveals a great similarity in their appearance. The skin is thin, dry, and glossy, and the facies is somewhat suggestive of congenital syphilis. Frontal bossing is prominent, the supraorbital ridges are high and wide, the nasal bridge depressed, the lips thick and protruding, the teeth absent or deficient, and the nails normal or dystrophic.

Cases have been reported of absence of mammary glands, chiefly in females, unassociated with any of the other stigmas of ectodermal defect. In a review of the literature 10 cases [2] of unilateral absence were found and five cases [3] of bilateral absence. In addition, Dr. Robert Owen [4] told me of a private patient whom he saw in 1950, a 30-year-old white man, a native of Venezuela, who had no nipples, but who had no other ectodermal defects. However, these cases are not instances of the syndrome of ectodermal defect.

REPORT OF A CASE

R. M., a Negro boy aged 16 months, was admitted to Gallinger Municipal Hospital on July 16, 1948, because of diarrhea and a positive Kahn reaction. The diarrhea responded to symptomatic therapy. Results of repeated serological tests for syphilis were negative, and the child was discharged without further treatment. He was admitted to Children's Hospital on Oct. 15, 1948, because of an upper respiratory infection. This infection was found to be tuberculous bronchopneumonia, and improvement followed treatment with streptomycin and dihydrostreptomycin. He was transferred to Glenn Dale Tuberculosis Sanatorium on Feb. 4, 1949, for convalescence.

History and Physical Examination.—The mother was treated for early latent syphilis during pregnancy with 3,000,000 units of penicillin in oil and wax; her last serological test for syphilis was still positive. The father was unknown. The mother knew of no inherited anomalies in her family. The child was obviously malnourished and had a very dry and scaly skin and a scalp devoid of any hair, except fine lanugo fuzz. There were no eyebrows or eyelashes. The supraorbital ridges were prominent. The nasal bridge was depressed, the lips were thick and everted, and no teeth were present. The chest was smooth, with no evidence of breast tissue or nipples. The nails and extremities were normal.

Laboratory and Sweating Studies.—The Kahn reaction was 1+ in July, 1948; repeated tests gave negative results over the next eight months. The spinal fluid was within normal limits. Roentgenograms of the chest were consistent with the clinical (medical) diagnosis. A roentgenogram of the mouth area did not show any evidence of teeth or any tooth buds (Fig. 2). Biopsy could not be performed. The child had never been noted to sweat; when he was placed under a heat cradle for 10 minutes, there was no sweating, but the body temperature rose about 1.5 F. Injection of pilocarpine and use of "quinizarin compound" (28% 2:6 disulphonic acid with sodium carbonate and cornstarch) failed to produce any sweating on several areas of body.

Chief Features of Reported Cases of Ectodermal Defect with Amastia

Case	Author	Date	Sex	Hair	Teeth	Skin	Nose	Sweating	Nails
1	Hutchinson	1886	M	Alopecia except lanugo hair	"Tolerably normal"	Thin, wrinkled, "old-mannish"	Not described	Not stated	Spoon-shaped
2	Tendlau	1902	M	Partial alopecia; beard, axilla, and pubis normal	4 in upper jaw; none in lower	Dry, thin, and scaly	Saddle; atrophic mucous membrane	Absent	Normal
3	Kaalund-Jorgensen	1941	M	Alopecia except lanugo hair and eyelashes	13; some deformed	Thin, fine, and dry	Saddle; atrophic mucous membrane	Absent	Normal
4	Upshaw and Montgomery	1949	M	Partial alopecia; beard normal	None	Keratoderma of palms and soles	Saddle; atrophic mucous membrane	Absent	Normal
5	Osbourn	1952	M	Alopecia except lanugo hair	None	Thin, dry, and scaly	Saddle	Absent	Normal

COMMENT

This case is the fifth to be reported in which absence of nipples and mammary glands is a part of the syndrome of congenital ectodermal defect. All the patients have been males; all have had absence of sweating and partial or complete absence of teeth. The chief features of these patients are listed in the table.

The clinical and pathological aspects of this syndrome have been adequately described in the excellent paper of Upshaw and Montgomery.[1d] The most disabling feature of the syndrome is the inability to sweat and the dry-

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The staff of the Tuberculosis Sanatorium (Glenn Dale Sanatorium), Glenn Dale, Md., particularly Dr. M. Weiss, assisted in the handling of this case.

1. (*a*) Hutchinson, J.: Congenital Absence of Hair and Mammary Glands, Proc. Roy. Med. & Chir. Soc. **69**: 493, 1886. (*b*) Tendlau, B.: Ueber angeborene und ervorbene Atrophia cutis idiopathica, Virchows Arch. f. path. Anat. **167**: 465, 1902. (*c*) Kaalund-Jørgensen, O., and Christensen, J. F.: Congenital Ectodermal Dysplasia of Anidrotic Type, Acta dermat.-venereol. **22**: 1, 1941. (*d*) Upshaw, B. Y., and Montgomery, H.: Hereditary Anhidrotic Ectodermal Dysplasia: A Clinical and Pathologic Study, Arch. Dermat. & Syph. **60**: 1170 (Dec.) 1949.

2. Whyte, G. D.: Congenital Absence of Breast, Lancet **2**: 1249, 1904. Schneller, E. W.: Congenital Amazia, M. Rec. **53**: 282, 1898. Viégas, A. P.: Amastia referencia de un caso, Brasil-med. **62**: 201, 1948. Simard, René: Sur un cas d'amastie, Laval méd. **13**: 687, 1948. Bertone, C.: Amastía unilaterale e deformità di une mano nello stesso soggetto, Rinasc. Med. **7**: 548, 1930. Louria, H. W.: A Case of Unilateral Amastia, Am. J. Obst. **8**: 364, 1924. Putzu Doneddu, F.: Un caso di amastia monolaterale, Arch. ostet. e ginec. 2 Ser. **21**: 1, 1934. Lutaud, P.: Sur un cas d'amastie et brachydactylie, Arch. gén. de méd. 467, 1910. Gilly, E.: Absence complète de mamelles chez une femme mère: atrophie du membre supérieur droit, Courier méd. **32**: 27, 1882. Paull, F.: Total Absence of the Left Mammary Gland, from Nondevelopment, Lancet **1**: 648, 1862.

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ness of the skin from lack of sebaceous glands. Obviously, there is no curative treatment, but it is important that such cases be diagnosed early and the heat regulation carefully watched by nurses or parents of the patient. As the child grows, he should be taught to watch his own heat regulation by avoiding hot foods and beverages in excess and strenuous exercise in a hot environment. In one case reported by Upshaw and Montgomery [1d] the patient was able to obtain gainful employment as a lifeguard.

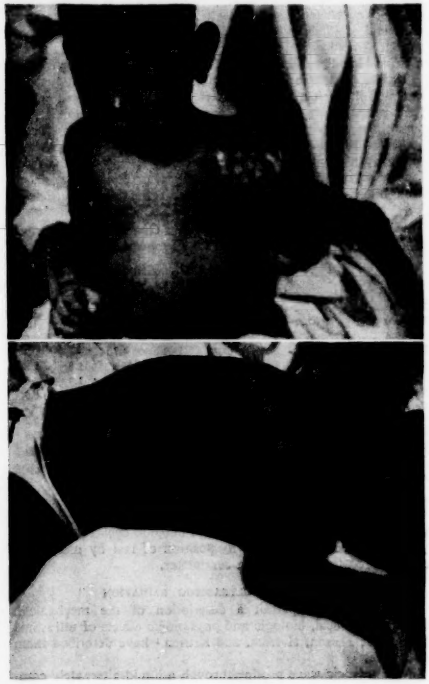

Fig. 1.—Patient in case reported, showing absence of nipples, saddle nose, prominent frontal bossing, thick, protruding lips, and lanugo fuzz.

The lack of sebaceous gland activity interdicts the usual use of soap and water. One of the superfatted soaps may be tolerated, if it is used in small amounts, or possibly one of the soap substitutes, such as oily pHisoderm® or a surface-acting detergent (terjolate®), may be suitable for cleansing. Further, the regular use of some bland oil, such as olive oil, baby oil, theobroma oil (cocoa butter), or "nivea" skin oil (cholesterolized petrolatum in a water emulsion with eucerite), will keep the skin lubricated and help to prevent dryness, scaling, and fissuring.

Patients who have dental aplasia, as the patient in this case, should have early dental care. The consensus of the dentists I have consulted about this case is that complete dentures should be made as soon as it is possible to get the necessary cooperation of the patient. In the case reported by Israel,[5] full dentures were made for a child aged 4 to replace lost and infected deciduous teeth and roots; these apparently were completely satisfactory and were to be removed as the permanent teeth erupted. McBride [6] advises the use of dentures in young children where they are indicated; he records the use of partial dentures in a child aged 4 and a full upper denture in a child aged 5. Full dentures were made by Bray [7] for an edentulous child 13 years of age.

SUMMARY

The case of a Negro boy with congenital absence of nipples and breasts as a part of congenital ectodermal defect, further characterized by alopecia, dry, scaly skin, saddle nose, and complete absence of teeth, is reported. Comparison of the reported cases of such defect is made in tabular form. Suggestions for symptomatic management of patients with ectodermal defect, particularly to regulate body temperature and lubricate the skin, are given.

Fig. 2.—Head of patient in case reported, showing absence of teeth.

Columbia Medical Building, 1835 Eye St., N. W.

3. Wylie, W.: Case of Entire Absence of Both Mammae in a Female Aged 21 Years, Brit. M. J. **2**: 235, 1888. Batchelor, H. T.: Absence of Mammae in a Woman, ibid. **2**: 876, 1888. Glos, J.: Bilateral Amazia with Malformation of Extremities, Časop. lék. česk. **71**: 865, 1932. Ray, D. S.: Complete Absence of Breast in a Female, St. Barth. Hosp. J. **27**: 158, 1919-1920. Liebenam, L.: Zwillingspathologische Untersuchungen aus dem Gebiet der Anomalien der Körperform. Partieller Riesenwuchs. Angeborener Pectoralisdefekt. Dysostosis cleidocranialis. Dysostis craniofacialis, Ztschr. f. menschl., Vererb. u. Konstitutionslehre **22**: 373, 1938.

4. Owen, R.: Personal communication to the author.

5. Israel, W.: Dental Foci of Infection and Full Dentures for Children, J. Southern California State Dent. A. **16**: 27, 1949.

6. McBride, W. C.: Juvenile Dentistry, Philadelphia, Lea & Febiger, 1945.

7. Bray, C., cited by McBride.[6]

Carcinoma of the Breast.—Carcinomas still limited to the confines of the breast are usually clinically indistinguishable from benign tumors, hence their clinical diagnosis is for all practical purposes the diagnosis of dominant lump. A dominant lump is one which varies from anything else felt in the breasts in size, consistency and differentiation from surrounding tissue. Between one third and one half of all such lumps are carcinoma. . . . —Louis P. River, M.D.; Joseph Silverstein, M.D., and Eugene F. Dolehide, M.D., Carcinoma of the Breast, Symptoms and Diagnosis, *The Journal of the Iowa State Medical Society*, December, 1951.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

RALPH E. DE FOREST, M.D., *Secretary.*

PRESENT STATUS OF USE OF ULTRASONIC ENERGY IN PHYSICAL MEDICINE

The study of ultrasonic energy as a separate science began only a little more than 30 years ago, when high frequency acoustic vibrations were first employed for underwater communication. (This led to the development of "sonar" during World War II.) Since these studies began, several thousand articles on various applications of ultrasonic energy have been published and within the last few years hundreds of artieles have been written concerning the medical applications of ultrasonic energy. Most of the articles on the medical employment of ultrasonic energy have been published in Europe, particularly in Germany and Austria, and until recently American physicians have shown little interest in this field. There has been an unfortunate exploitation of devices for ultrasonic therapy in Europe just as there was an exploitation of short wave diathermy devices about 15 years ago.

About 1935 the European medical literature, particularly the German and Austrian, was filled with exaggerated and uncritical claims concerning the value of short wave diathermy in a wide variety of diseases. Claims were made that short wave diathermy would be of value in the treatment of malignancy and it was also contended that these short wave electrical radiations had a number of effects other than those attributable to heating of tissues. Soon European short wave diathermy machines were being imported into the United States in large numbers and American manufacturers began producing them in even larger quantities. It took several years for careful medical investigators here and abroad to overcome this early exploitation of short wave diathermy, to define its limitations and to indicate its proper sphere of usefulness in medicine.

Now history is repeating itself with regard to the employment of ultrasonic energy. These ultrasonic devices are being exploited in Europe; exaggerated claims concerning their value in a wide variety of diseases are being made. It has been claimed by certain German physicians that ultrasonic energy is of value in the treatment of malignancy and they are also claiming mysterious effects other than those attributable to heating of tissues. Importations are now being made from Europe, and American manufacturers also are starting to make ultrasonic apparatus for use in medicine.

If ultrasonic energy is employed properly by skilled physicians and not used indiscriminately as a "cure-all," it offers promise of becoming a valuable new therapeutic and diagnostic agent. Therefore, it is important for American physicians to familiarize themselves with these ultrasonic machines, to examine critically the evidence concerning their possible diagnostic or therapeutic usefulness, and to determine promptly the limitations and dangers of ultrasonic therapy. Already it is apparent that the therapeutic application of ultrasonic energy may cause damage of an irreversible nature to certain tissues of the human body and that overdoses of ultrasonic energy are potentially dangerous. The margin of safety is much less with ultrasonic diathermy than with short wave diathermy.

ULTRASONIC APPARATUS

Commonly, ultrasonic vibrations are produced by using a piezo-electric crystal. Certain crystals such as quartz will become electrically charged on opposite surfaces when they are subjected to mechanical pressure. This property is called the "piezo-electric effect." The reverse effect also occurs, and the crystal will undergo mechanical vibration when opposite sides are subjected to an alternating electric field. It is comparatively easy to construct a piezo-electric transducer which converts electrical oscillations into mechanical vibrations which, in turn, produce sound waves. Such vibrations can be transmitted through a "sound head" to the surface of the body which is to be treated.

Unlike electromagnetic vibrations, ultrasonic radiations cannot pass through a vacuum but require a material medium for their propagation. These ultrasonic waves travel approximately four times as fast in liquids, and up to twenty times as fast in solids, as they travel in air. High frequency sound waves tend to travel in straight lines, are completely reflected at the interface between two mediums if the critical angle is exceeded, exhibit interference phenomena and are refracted. A particle in the field is forced to vibrate through 800,000 cycles per second, yet it is not displaced from its position of rest by more than one-hundred thousandth of a centimeter.

TABLE 1.—*Diseases Treated and Results Obtained by Ultrasonic Therapy as Presented by Two European Physicians**

Diagnosis	Cases	Results of Treatment, % †				
		++	+	0	−	?
Herpes zoster	51	55.0	19.5	23.5	—	2.0
Intercostal neuralgia	128	58.6	22.7	17.1	—	1.6
Sciatica	1,508	62.0	22.6	10.3	0.5	4.6
Lumbago	213	67.7	18.2	4.7	—	9.4
Multiple sclerosis	106	2.8	42.5	49.1	2.8	2.8
Myalgias	99	39.5	49.5	5.0	1.0	5.0
Neuralgias	852	60.2	21.5	10.1	0.6	6.6
Periarthritis (humeroscapular)	177	35.5	43.0	15.2	1.1	5.2
Spondylitis (deforming)	273	36.6	49.5	9.1	2.2	2.6
Trigeminal neuralgia	128	18.0	32.8	40.7	3.9	4.6

* From Matthes, K. and Rech, W.: Der Ultraschall in der Medizin. Zürich, S. Hirzel Verlag, 1949, 485 pp.
† Result best = ++; result next best = +; no benefit = 0; condition worse = −; result questionable = ?.

EFFECTS OF ULTRASONIC RADIATION

Space does not permit a description of the mechanical, thermal, chemical, biologic and physiologic effects of ultrasonic energy but Nelson, Herrick, and Krusen [1] have described them elsewhere.

An ultrasonic wave passing through a liquid alternately compresses and separates its component particles and with high enough intensity the disruptive forces exceed the intermolecular bonds and the medium is actually split apart. This phenomenon, which involves not only the formation of cavities but also their sudden collapse, is called "cavitation."

Freundlich, Söllner, and Rogowski [2] concluded that bone marrow could be strongly heated by ultrasonic radiation; therefore, they expressed the belief that the therapeutic possibilities of ultrasonic diathermy merited further study. Many European clinicians have mentioned an "analgesic effect" of ultrasonic radiation.

In Table 1 are listed a number of diseases in which ultrasonic therapy has been employed by European physicians. It will be noted that the largest number of cases treated represented sciatica and neuralgia; also that a high percentage of beneficial results was reported.

European physicians, led by Pohlman,[3] have concluded that an intensity of ultrasonic radiation of 2 to 5 watts per square centimeter, which produced erythema without edema, is the correct dose for treatment. A frequency of 800,000 cycles per second appears to be most satisfactory for therapy. This is the frequency we have used in our experiments.

This report is a summary of work performed by the following investigators of the Mayo Clinic and Mayo Foundation, Rochester, Minn.: Frank H. Krusen, M.D., Section of Physical Medicine and Rehabilitation; J. F. Herrick, Ph.D., Carl F. Schlotthauer, D.V.M., and Khalil G. Wakim, M.D., Ph.D., Division of Experimental Medicine; Warren A. Bennett, M.D., Section of Pathologic Anatomy, Joseph M. Janes, M.D., Section of Orthopedic Surgery; Edward H. Lambert, M.D., Ph.D., Section of Physiology; and Paul A. Nelson, M.D., Thomas P. Anderson, M.D., Ralph E. De Forest, M.D., and Walter J. Treanor, M.B., Fellows in Physical Medicine and Rehabilitation.

1. Nelson, P. A.; Herrick, J. F., and Krusen, F. H.: Ultrasonics in Medicine, Arch. Phys. Med. **31**: 6-19 (Jan.) 1950.

2. Freundlich, H.; Söllner, K., and Rogowski, F.: Einige biologische Wirkungen von Ultraschallwellen, Klin. Wchnschr. **11**: 1512-1513 (Sept.) 1932.

3. Pohlman, Reimar: Die Ultraschalltherapie: Quantitative Angaben zu ihrem Wirkungsmechanismus, Deutsche med. Wchnschr. **73**: 373-377 (Sept. 3) 1948.

On the completion of our original survey, three of us, Nelson, Herrick, and Krusen,[1] concluded that, despite enthusiastic claims of some European investigators, enough was not known concerning the physiologic effects of ultrasonic energy to warrant its use in treatment of any disease of man. Nevertheless, we concluded that the diagnostic and therapeutic possibilities of ultrasonic energy merited further careful scientific evaluation. Since then, we have sought further evaluation by suitable labo-

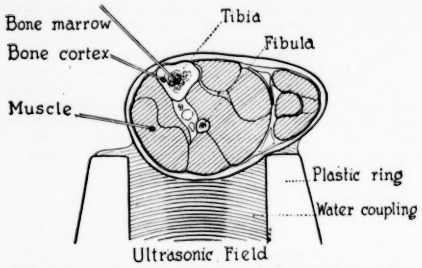

Fig. 1.—Cross section showing placement of thermistors in the hind leg of an anesthetized dog for measurement of the heating effects of ultrasonic energy on bone marrow, bone and muscle.

ratory studies on living animals. First, mindful of the report of Freundlich and his associates,[2] we asked ourselves the following questions:

What relative heating can be produced by ultrasonic radiation in living tissues such as bone marrow, bone cortex and muscle? Might ultrasonic radiation prove to be a useful form of medical diathermy? In attempting to answer these questions, three of us (Nelson, Herrick, and Krusen [4]) used a small, efficient ultrasonic generator, made by the Central Research Laboratories, and producing a maximal output of 15 watts. The area of the crystal used in this apparatus is approximately 5 sq. cm. We also obtained from Germany a Siemens "Sonostat," which delivered up to 60 watts of ultrasonic energy. In this device a piezo-electric crystal with an area of 10 sq. cm. is mounted in a grounded metal unit, which is called the appli-

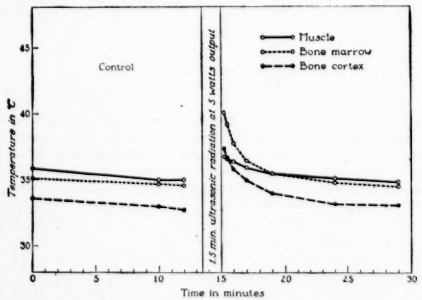

Fig. 2.—Temperatures produced by the application of ultrasonic energy to the lateral surface of the hind leg of an anesthetized dog. Data obtained in a typical run in which an exposure was made for 1.5 minutes at an output of 5 watts.

cator or "sound head," in such a way that the mechanical vibrations (ultrasonic waves) are conducted through a metal diaphragm.

Temperatures of bone marrow, bone cortex and muscle were measured with thermistors or by thermocouples. Figure 1 shows how the thermistors were placed in the bone marrow, bone cortex, and muscle of the hind leg of an anesthetized dog; Figure 2 shows a typical observation in which there was a marked increase in the temperature of bone marrow when ultrasonic radiation was applied to the lateral surface of the dog's hind leg for one and one-half minutes at an output of 5 watts.

Table 2 shows the marked rises in temperature produced in bone marrow and bone cortex in only one and one-half minutes.

It will be noted that in these anesthetized dogs, if the wattage was increased from 5 to 10, the rise in temperature nearly doubled. After only one and one-half minutes of ultrasonic radiation at an output of 5 watts, rises of temperature of bone cortex and bone marrow were slightly greater than those obtained after 30 minutes of microwave radiation at an output of 65 watts. No observable gross damage to superficial tissues was noted following either microwave or ultrasonic radiation.

It was concluded that ultrasonic radiation can produce sharply localized heating of living tissues and can cause selective heating of bone cortex and bone marrow as does no other source of energy used thus far for medical diathermy, and further that if ultrasonic diathermy is administered clinically, a wide margin of safety with regard to dosage is necessary because of unexpected variations which frequently arise.

After completing this study, we next asked ourselves the question:

What are the effects of ultrasonic energy on the nervous system? To answer this question, Anderson, Wakim, Herrick, Bennett, and Krusen [5] initiated studies on the lower part of the

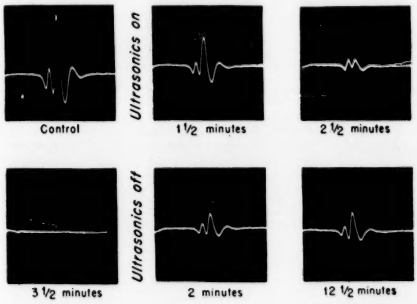

Fig. 3.—Effect of application of ultrasonic energy on the action potential of the sciatic nerve.

spinal cord and on peripheral nerves of living dogs. Clinical observation of paralysis and observation of alteration of action potentials of nerves were made. Temperatures produced by ultrasonic energy were studied and histopathologic changes in the nerve resulting from ultrasonics were also reported. Maximal doses were employed.

Studies of the effect of application of ultrasonic energy on action potentials were particularly interesting. Figure 3 shows the reduction to zero (complete block), such as occurred in 8 of 12 dogs within 10 minutes or less (in this case within 3½ minutes) and the partial recovery thereafter. It was then found that the action potential of the sciatic nerve was decreased by direct heating in a strikingly similar manner.

The range of temperature (measured in the sheath of the sciatic nerve) at which the action potential becomes decreased was found to be narrow, i. e., between 48 and 52 C. If the action potential was only partially decreased recovery usually was complete, whereas if the action potential was completely flattened, there was usually only partial or no recovery.

Marked destruction occurred in every dog which exhibited paralysis following application of ultrasonic energy over the

4. Nelson, P. A.; Herrick, J. F., and Krusen, F. H.: Temperatures Produced in Bone Marrow, Bone, and Adjacent Tissues by Ultrasonic Diathermy: An Experimental Study, Arch. Phys. Med. **31**: 687-695 (Nov.) 1950.

5. Anderson, T. P., and others: An Experimental Study of the Effects of Ultrasonic Energy on the Lower Part of the Spinal Cord and Peripheral Nerves, Arch. Phys. Med. **32**: 71-83 (Feb.) 1951.

spinal cord. Figure 4 shows the severe necrosis and marked gross pathologic changes found in one such animal. Figure 5 is a photomicrograph showing normal muscle surrounding a nerve in which marked degenerative changes have been produced by local application of ultrasonic radiation.

On completion of these studies we concluded that ultrasonic energy applied in maximal doses over the lower vertebrae of dogs resulted in paralysis of the hind legs and tail. Furthermore,

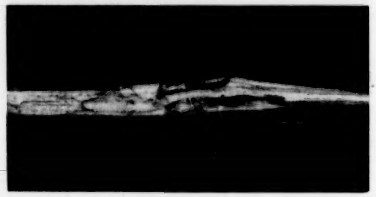

Fig. 4.—Gross appearance of the spinal cord of a dog which was exposed to ultrasonic energy in a dosage of 5 watts per square centimeter applied for 10 minutes over the upper lumbar vertebrae. Complete paralysis of the legs and tail ensued. At necropsy severe necrosis and other gross pathologic changes were found

ultrasonic energy in the amount of 3.0 to 5.8 watts per square centimeter, applied to the mid-thigh, resulted in complete blocking of, or at least 50% decrease in, the action potential of the intact sciatic nerve in 60% of the dogs studied. Recovery, as indicated by the action potential, was usually complete when the action potential had been only partially decreased by the

Fig. 5.—Photomicrograph of section of small nerve in a superficial muscle of a rat three weeks after direct exposure to ultrasonic energy. Although the nerve exhibited the unusual regular pattern of myelin degeneration which was commonly produced by ultrasonic energy, no evidence of change could be seen in the muscle surrounding the nerve.

ultrasonic energy but recovery was generally incomplete when the amplitude of the action potential had been completely flattened. Direct heating produced a strikingly similar effect on the action potentials. Ultrasonic energy had much greater destructive effect on the spinal cord than on the sciatic nerve.

Following a lead developed in this study on nerves, we asked ourselves another question:

What are the relative effects of heat and ultrasound on conduction of nerves? (Are the effects of ultrasound on peripheral nerves owing entirely to heat or do the effects differ from those caused by conductive heating?) Treanor, Lambert, Herrick, and Krusen [6] continued this study by irradiating the sciatic nerve of a bullfrog between stimulating and pick-up electrodes at a level of 4 watts per square centimeter. The effect is illustrated in Figure 6. The upper curve shows the temperature of the nerve bath and below are the sound curves indicating the amplitude of the "A" and "B" spikes of the nerve action potential. The periods of irradiation with ultrasound are shown by the upper bar. The periods of cooling of the bath by circulation of fluid through it are shown by the lower bar.

TABLE 2.—*Results Obtained on Experimental Heating of Tissues of Hind Legs of Anesthetized Dogs**

Wattage	Runs	Tissue	Average Rise in Temperature, C.
5	13	Bone marrow	5.39
		Bone cortex	5.92
		Muscle	1.12
10	9	Bone marrow	10.29
		Bone cortex	10.50
		Muscle	2.21

* Data obtained 15 seconds after exposure for 1.5 minutes to ultrasonic radiation. (Note that the temperature of bone marrow and bone cortex were increased in only 1.5 minutes to high levels and that when the wattage was increased from 5 to 10, these increases were nearly doubled.)

TABLE 3.—*Comparison of Effects of Direct Heating (Thermode) and Ultrasonic Energy on Production of Conduction Block in Various Fiber Groups of Sciatic Nerve*

		Fiber Group *				
		A			B	C
		α	β	γ		
Thermode	°C.	45.4 ± 0.1‡	45.6 ± 0.1	45.6 ± 0.3	43.5 ± 0.1	45.1 ± 0.1
	n	15	12	10	19	12
Ultrasound	°C.	45.5 ± 0.3	45.5 ± 0.3	45.7 ± 0.3	43.4 ± 0.2	44.8 ± 0.2
	n	9	8	7	18	11
Difference †		− 0.1 ± 0.3	0.1 ± 0.3	− 0.1 ± 0.4	0.1 ± 0.2	0.3 ± 0.2

* Sciatic nerve of Rana catesbiana.
† Mean and its standard error.
‡ Note that the differences are negligible.
N—Number of experiments.

When the temperature of the bath was allowed to rise by stopping the circulation of the coolant, decrease of the action potential occurred, indicating a block of conduction in some fibers. When the temperature was maintained at a low level, there was no apparent effect of the ultrasound over long periods of time. Note also that there was some evidence of a differential effect on "A" and "B" fiber groups. It seemed desirable to determine whether the effects of ultrasound on peripheral nerves were owing entirely to a rise in temperature of the nerve or whether the effects of ultrasound occur at lower temperatures than those of heat alone. Experiments indicated that ultrasound of intensities and frequencies employed in physical medicine at the present time has no effects on conduction in peripheral nerves other than those produced by the rise of temperature.

The data which are summarized in Table 3 indicated that the temperature at which complete block of fiber groups occurred was essentially the same whether heating was produced by thermode or by ultrasound. This warrants the conclusion that ultrasound of intensities and frequencies employed in physical medicine probably has no effects on conduction in peripheral nerve other than those produced by the rise of temperature. It is of interest also that the differential effects of heat on the nerve do not suggest an explanation of the so-called analgesic effects of heat.

6. Treanor, W. J.; Lambert, E. H.; Herrick, J. F., and Krusen, F. H.: Comparative Study of the Effects of Heat and Ultrasound on Nerve Conduction, unpublished data.

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Next we asked ourselves the following question:

What are the effects of ultrasound on the growing ends of long bones? To answer this question, De Forest, Janes, Herrick, and Krusen [7] studied the effect of ultrasonic energy on the hind legs of dogs which were 4 to 6 months old. The dogs in these new experiments were anesthetized, and the sound head was kept moving to minimize the effect of standing waves and to distribute the radiation better throughout the bone. The medial surface of the leg over the upper tibial epiphysial region was placed on a plastic applicator filled with degassed water from a reservoir bottle. This water served as the coupling medium between the sound head and the animal's leg.

Figure 7 shows the result when eleven ultrasonic applications of 10 watts for five minutes were given to one young dog. Eleven weeks after the last application, the roentgenogram was made. It shows obliteration of the lateral half of the upper tibial epiphysial line, destruction of the medial part of the medial tibial plateau, erosion of the surface of the medial condyle of the femur, and partial obliteration of the lower femoral epiphysial line.

Four ultrasonic applications of 10 watts for 10 minutes were given to another young dog, and two weeks later a fifth application was made (Fig. 8). Nine weeks and three days after this last application there was obliteration of the upper tibial epiphysial line in its lateral half, destruction with partial resorption of the upper tibial epiphysis, rarefaction in the condyles of the femur, obliteration of the lower femoral epiphysial line,

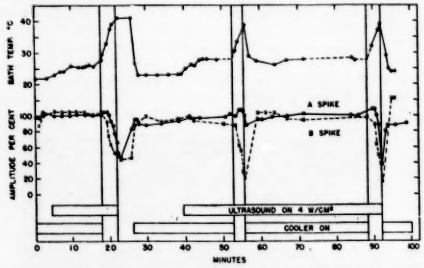

Fig. 6.—Effect on the "A" and "B" spikes of the action potential of the sciatic nerve produced by varying the temperature of a bath in which the nerve was placed and by applying ultrasonic energy to the nerve. (See the text for further explanation.)

dislocation of the knee joint, and swelling of the soft tissues.

It was obvious that ultrasound is very destructive to the growing bones of the dog when administered in the manner and doses described. Until safe dosages are determined through further investigation, ultrasonic therapy should not be applied to growing bones.

Having completed these studies, we asked ourselves another question:

What are the histopathologic effects of ultrasound on tumors? Bennett, Herrick, Schlotthauer, and Krusen [8] conducted these studies. First, we studied the effect on a transmissible lymphosarcoma originated by Carl Olsen, Jr. Figure 9 shows a cross section made by freezing an entire chicken and sawing across it, thus giving this picture of the viscera and the treated tumor. This tumor had been injected into the breast five days before treatment. This chicken was treated for 30 minutes at 15 watts on two occasions. The necrosis of the skin and underlying tumor is well outlined. The solid mass infiltrating the muscle is the remaining portion of the tumor.

When a transmissible glioma of the ependymona type, in a mouse, was treated for 75 seconds with 15 watts, there was a large amount of necrosis, but still much viable tumor remained.

When a Walker carcinoma in a rat was treated with 20 watts for 10 minutes, there was focal necrosis of skin, muscle, and tumor, and when a spontaneous squamous cell carcinoma of a dog was treated with ultrasound for 30 minutes at 15 watts, there was necrosis of the tumor but there was also much viable tumor remaining.

When a plasma cell myeloma of a dog was treated for 30 minutes with 15 watts, there was superficial necrosis but little or no effect on the tumor.

Fig. 7.—Roentgenogram showing the damage done to the bones of the hind leg of a young dog following 11 applications of ultrasonic energy of 10 watts for five minutes each. (See the text for further explanation.)

Fig. 8 *a* and *b*.—Roentgenograms showing the damage done to the bones of the hind leg of a young dog following five applications of ultrasonic energy of 10 watts for 10 minutes each. (See the text for further explanation.)

It was concluded that among the tumors treated there was no demonstrable selective action. There was as much destruction of

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normal tissues as there was of the tumor. It was possible to cause necrosis at will in the tumors but never possible to destroy them completely.

We then asked ourselves one final question:

What are the histopathologic effects of ultrasound on normal tissues? When normal chicken liver was exposed to a maximal dose of ultrasonic energy, there was necrosis immediately beneath the breastbone. The energy had penetrated the bony structure. When the skin of a dog was examined microscopically three days after an application of 25 watts for four minutes, there was ulceration of the epidermis, with necrosis of all elements including the muscle.

Fig. 9.—Cross section of a chicken showing the gross appearance following two applications of ultrasonic energy of 15 watts for 30 minutes. The energy was applied to skin over a transmissible lymphosarcoma of the breast. Evidence of necrosis of the skin and of part of the tumor can be seen but much viable tumor remains. (See the text for further explanation.)

We found that there was a selective destruction of hair follicles just as there was selective destruction of nerve tissue. Figure 10 shows, for comparison, normal dog testes. Figure 11 shows dog testes following one treatment of 15 watts for thirty minutes. There is marked destruction of all cells except the basal elements in the seminiferous tubules. When the intestine of a rat was examined one hour after a treatment with 20 watts for 10 minutes, it was noted that there was diffuse necrosis throughout the thickness of the wall of the intestine. This occurred at the point of a gas bubble in the intestine, which acted as a barrier, with reflection of the ultrasonic energy so that this part of the intestine was severely damaged by the extra exposure caused by the combination of the original and the reflected radiation.

The skin exhibited an initial reaction of hyperemia followed by edema of the epidermis and dermis and the necrosis and formation of blebs. This necrosis often extended into the muscle.

The changes in the muscles included edema and interstitial hemorrhage followed by degeneration of the fibers, increase in sarcolemma cells, and a hemorrhagic appearance of the fibers. Finally, collapse of the muscle fibers was noted. If this collapse did not occur, then there was calcification of the degenerated fibers.

Necrosis of the spinal cord was marked throughout its entire thickness. There was extensive destruction of myelin and of all the elements of the cord. This resulted in complete paralysis, with marked necrosis and early phagocytic reaction.

The nerve fibers showed myelin degeneration, which often was patchy. In other areas it was rather diffuse. Accompanying the myelin destruction there were swelling and lobulation of the axons. Nerves may be markedly involved in the center of masses of muscle which show little or no change.

In mature bone there was fragmentation of the trabeculae with hemorrhage and destruction of the marrow. In immature bone there was erratic growth of cartilage, which was irregularly ossified. The marrow also was markedly destroyed.

It was concluded that ultrasonic energy can produce markedly destructive reactions in tissues, occurring at the point of application of the ultrasonic energy, throughout the pathway of the radiation through the tissues, or at the point of exit. The intensity of the destructive effects varies according to the type and density of the tissues or according to the presence or absence of fascial barriers. The reactions obtained in various animals were similar and varied not with the animal but with the intensity and duration of the treatment.

GENERAL CONCLUSIONS AND COMMENT

Throughout all of these studies maximal dosages usually were employed. Yet, except in one study, the dosages did not exceed even half those available on one of the machines which is commonly employed by physicians. The maximal dosage we employed (except in a few instances) was 25 watts for 30 minutes. The machine is capable of providing 60 watts for indefinite periods of time. It is apparent that such a machine, employed at maximal dosages, can severely damage many types of tissues; the spinal cord, peripheral nerves, testes, growing bones, and hair follicles appear to be particularly susceptible to damage.

Fig. 10.—Photomicrograph of section of normal testis of a dog. (For comparison with Figure 11.)

The danger of intensification of dosage by reflection must always be considered. The effects of ultrasonic energy on living tissues appear to be chiefly those of heating.

Having explored, rather fully, the effects of maximal dosages of ultrasonic energy on living animals, we now propose to investigate the effects of smaller dosages and to attempt to ascer-

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tain what the optimal dosages, if any, may be. It is certain that ultrasonic energy is a potent destructive agent which may be extremely dangerous if employed indiscriminately by unskilled persons. Nevertheless, continued laboratory investigations of the therapeutic and diagnostic possibilities of this new and potent physical agent assuredly are justified.

Fig. 11.—Photomicrograph of section of testis of a dog following one exposure to ultrasonic energy of 15 watts for 30 minutes. (Note the marked destruction of all cells except the basal elements of the seminiferous tubules.)

The medical diagnostic possibilities of ultrasonic energy are intriguing. Ludwig and Struthers [9] at the Naval Medical Research Center in Bethesda, Md., have developed a technique for locating nonradiopaque gallstones and foreign bodies at operation by ultrasonic means. Wild [10] at the University of Minnesota School of Medicine has devised a method of measuring the thickness of the intestinal mucosa by ultrasonic methods and Hueter and Bolt,[11] working at the Massachusetts Institute of Technology, have developed a procedure for performing ventriculography by ultrasonic means (sonography).

Many potent therapeutic agents are dangerous in overdoses. When no anesthesia is employed, pain will serve as a protective mechanism for prevention of overheating of tissues. With proper dosage, ultrasonic diathermy may produce valuable selective heating effects not previously obtainable. It is recognized that ultrasound may produce effects, other than thermal ones, on the tissues. However, the effects are obviously chiefly those of heating and there is no need for ultrasound to produce other mysterious effects for it to be of value in therapy.

Although many hundreds of patients have been treated with ultrasound, particularly in Europe, apparently without harmful effects, it is believed that physicians should await further cautious study of ultrasonic therapy before using it indiscriminately in clinical practice.

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COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Acet-Dia-Mer-Sulfonamides (See THE JOURNAL, Oct. 20, 1951, page 759).

Suspension Dorsulfas: 473 cc. bottles. A suspension containing 33 mg. each of sulfacetamide, sulfadiazine, and sulfamerazine in each cubic centimeter. Smith-Dorsey Company, Lincoln, Neb.

Tablets Dorsulfas: 0.5 gm. Each tablet contains 0.167 gm. each of sulfacetamide, sulfadiazine, and sulfamerazine. Smith-Dorsey Company, Lincoln, Neb.

Aminophylline-U.S.P. (See New and Nonofficial Remedies 1951, page 299).

Tablets Aminophylline: 0.2 gm., enteric coated. Keith-Victor Pharmacal Company, St. Louis.

Caprylic Compound (See New and Nonofficial Remedies 1951, page 45).

Vaginal Creme Naprylate: 90 gm. tubes. A cream containing 0.1 gm. of sodium caprylate and 50 mg. of zinc caprylate in a water miscible base. Packaged with a plunger-type applicator. R. J. Strasenburgh Company, Rochester, N. Y.

Choline Dihydrogen Citrate (See New and Nonofficial Remedies 1951, page 411).

Tablets Choline Dihydrogen Citrate: 0.65 gm. Physicians' Drug & Supply Company, Philadelphia, Pa.

Diethylstilbestrol-U.S.P. (See New and Nonofficial Remedies 1951, page 340).

Tablets Diethylstilbestrol: 1 mg. and 5 mg. uncoated. 0.25 mg., 0.5 mg., 1 mg., and 5 mg. sugar coated. Chicago Pharmacal Company, Chicago.

Folic Acid-U.S.P. (See New and Nonofficial Remedies 1951, page 440).

Tablets Folic Acid: 5 mg. Physicians' Drug & Supply Company, Philadelphia.

Neostigmine Methylsulfate-U.S.P. (See New and Nonofficial Remedies 1951, page 184).

Solution Neostigmine Methylsulfate 1:2000: 1 cc. ampuls. E. S. Miller Laboratories, Inc., Los Angeles, Calif.

Paramethadione (See New and Nonofficial Remedies 1951, page 256).

Capsules Paradione: 0.15 gm. Abbott Laboratories, North Chicago, Ill.

Phenylephrine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1951, page 198).

Solution Neo-Synephrine Hydrochloride 0.5% (Intranasal): 30 cc. bottles. A buffered isotonic solution containing 0.5 gm. of phenylephrine hydrochloride in each cubic centimeter. Preserved with 0.02% methylparaben, 0.01% propylparaben, and 0.2% sodium bisulfite. Winthrop-Stearns, Inc., New York.

Sulfadiazine-U.S.P. (See New and Nonofficial Remedies 1951, page 96).

Tablets Sulfadiazine: 0.5 gm. Mallard, Inc., Detroit, Mich.

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AORTOGRAPHY

Reinaldo Dos Santos, a Portuguese urologist, reported in 1929 before the Surgical Society of Paris his technique of translumbar aortography and clinical experiences with this method of visualizing the abdominal aorta, its branches, and the arteries of the lower extremities. Dos Santos performed 300 abdominal aortographies without an accident. He later reported one instance of bleeding in 1,500 cases. In a recent review of the experiences with this method at the Presbyterian Hospital in New York City, Deterling[1] reports no mortality in 100 aortographies. The needle hole readily seals itself because of the elasticity and thickness of the arterial wall. No hemorrhage was observed. Puncture through an atheromatous plaque is but rarely a cause of complication. The morbidity was minimal following injection of organic iodides.

Wagner and Price [2] reported one fatality in their series of 50 abdominal aortographies. This was due to the needle entering the superior mesenteric artery, which then received all of the iodide solution intended for the abdominal aorta, with resulting mesenteric thrombosis. Nelson [3] was first in this country to perform translumbar aortography. He had no fatalities in more than 100 cases. Another urologist, Doss,[4] stated that one of the fundamental requirements for obtaining a satisfactory abdominal arteriogram is adequate concentration of the radiopaque medium within the artery at the instant the roentgenographic exposure is made. He designed a special apparatus capable of exerting 3 atmospheres (45 lb.) of pressure on the fluid to be injected. He confirmed Nelson's observation of obtaining satisfactory "renograms." Such a renogram made possible recognition of a number of pathological processes within the kidney, such as renal agenesia, renal duplication, renal ectopia, retroperitoneal tumors, renal neoplasia, and cysts of the kidney.

Wagner and his co-workers [5] described a slightly modified technique of abdominal arteriography in which they used a 15 cm., no. 18 gage needle and a hand syringe for injection. Indications for abdominal aortography are aneurysm of the aorta, aortic occlusion, peripheral vascular disease, abdominal tumors, hypertension, and hydronephrosis. They felt that, although they had no untoward results in 26 instances, the method was not without potential dangers. It should therefore be employed as a diagnostic adjunct by carefully trained personnel only after simpler and standard studies have failed to yield sufficient information. Price and Wagner [6] demonstrated a complete aortic block just below the origin of renal arteries in two patients. Diagnosis was made during life by direct translumbar aortic injection of radiopaque medium. Collateral blood supply in cases of obstruction of the abdominal aorta is mainly by anastomosis of the inferior with the superior epigastric arteries and by a paravertebral anastomosis of lumbar arteries. The most important anastomosis among the visceral arteries is that of the middle colic with the left colic, thus allowing the inferior mesenteric artery to receive blood from the superior mesenteric artery and preventing gangrene of the sigmoid.

Translumbar aortography, as developed by Dos Santos, has now been practiced in some 3,000 cases. The needle is inserted just below the 12th rib and 4 fingerbreadths to the left of the spinal processes. The opaque medium must be nontoxic, nonirritating, rapidly excreted, and nonhemolyzing. Sodium iodide, which is customarily employed, can produce iodism and allergic reactions. Iodopyracet (diodrast®) in 70% solution does not produce so good a picture of the smaller arteries but is satisfactory. The method should not be used in the presence of severe liver damage, nephritis, uremia, or sensitivity to iodides. Deterling states that injection of 1,000 cc. of isotonic sodium chloride solution and of 500 mg. of vitamin C intravenously immediately after the procedure prevents iodism. The method can be used with the patient under local anesthesia or with thiopental sodium (pentothal®) intravenously for general anesthesia.

Castellanos and Pereiras [7] introduced in 1937 the retrograde method of visualizing either the thoracic or the abdominal aorta. The thoracic aortography was accomplished through injection into the brachial artery. The abdominal aortography was performed by injecting the femoral artery under pressure. Somewhat later, Fariñas [8] reported injecting the abdominal aorta by a method in which the femoral artery was exposed and 50 cc. of a 70% solution of iodopyracet was injected with a trocar within two and one-half and three seconds. The injection is made with a specially designed apparatus. In this country, Burford and Carson [9] utilized the left common carotid artery for demonstration of the anomalies or disease of the aorta and its immediate branches. They considered the method safe, dependable, and effective in the diagnosis of questionable cases of patent ductus arteriosus, coarctation of the aorta, and aortic arch anomalies. Goodwin and his associates [10] utilized a

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ureteral catheter, which was placed into the lateral circumflex branch of the profunda femoris artery and into the femoral artery up into the aorta. They felt, however, that the translumbar needle aortography is simpler, less hazardous, and should be the method of choice. Pearl and associates[11] passed a catheter into a peripheral artery and guided it under fluoroscopic control to the aorta and to many of its larger branches. They were able to demonstrate the coronary arteries.

The consensus is that translumbar needle aortography is safer and simpler than the retrograde catheter method. They are not regarded as routine diagnostic procedures but rather as diagnostic adjuncts in cases in which standard methods fail to reveal the lesion. Congenital anomalies of the heart, certain cardiovascular lesions, and lesions of the kidneys constitute the field in which the newer methods of arteriography will find their application.

LYSOZYME AND ULCERATIVE COLITIS

Since Meyer and his group,[1] in 1947, reported elevated fecal lysozyme concentrations in patients with ulcerative colitis, a number of studies of the possible role of lysozyme in the etiology of this disease have been reported. Recently, some investigators have cast doubt on the possibility that lysozyme may cause ulcerative colitis; but they emphasize the usefulness of the fecal lysozyme titer as an index of the degree of activity of the disease process.

Meyer's group[2] had previously observed that lysozyme was capable of removing the surface mucus from the stomach of a dog. Simultaneously they reported that in six patients lysozyme titers of gastric juice after vagectomy showed a mean fall of 44.4%, compared to preoperative levels, which suggests that lysozyme production is influenced at least in part by nervous control. They hypothesized that ulcerative colitis may be due to local overproduction of lysozyme followed by a necrotizing action on the mucosa by the indigenous bacterial flora. These workers subsequently produced ulceration of the stomach, small intestine, and colon in dogs by feeding lysozyme[3] and later reported almost uniformly high lysozyme content of the stools and mucosa in patients with ulcerative colitis. They also noted a fall in the lysozyme titers with clinical improvement.[4]

Portis,[5] recalling Meyer's hypothesis of the existence of a neural mechanism, suggested that increased emotional stimuli carried by the sacropelvic nerves may result in a high concentration of lysozyme in the colon leading to the loss of protective mucus. Grace and coworkers[6] found that, in normal subjects and in subjects with diarrhea but without ulceration, transitory elevations in fecal lysozyme often occurred in association with emotional upsets. In patients with ulcerative colitis, on the other hand, marked and sustained elevations of lysozyme occurred. The high titers immediately preceded exacerbations of colitis.

Glass[7] cast doubt on the etiological role of lysozyme when he reported that colonic mucus was not digested by lysozyme in vitro. He pointed out that the concentration of lysozyme used by Meyer to produce ulceration in the dog is higher than might be encountered in human pathological processes. Glass infers from his studies that, whatever the consequences of increased lysozyme in ulcerative colitis, they do not include digestion of the colonic mucus.

According to Gray,[8] prolonged inhibition of fecal lysozyme in six patients by oral administration of a detergent ("aerosol OT" [dioctyl sodium sulfosuccinate]) did not alter the course of the disease, which indicates that lysozyme does not play a significant role in the pathogenesis of ulcerative colitis. He reported that a profound decrease in fecal lysozyme, coincident with clinical improvement, occurred in all patients who responded to corticotropin (ACTH) therapy.[9] Gray believes the fecal lysozyme titer correlates with the amount of functioning tissue and its ability to respond to injury. In the presence of sufficient functioning tissue, the titer serves as an index of the activity of the disease process. Gray suggests that the decrease in fecal lysozyme following corticotropin therapy may be due to an inhibitory effect of corticotropin on the tissue's response to injury. He cautions, however, that inhibition of fecal lysozyme by a detergent does not necessarily reflect inactivation of the enzyme within the mucosal cells. Moreover, while lysozyme may not digest intraluminal mucus, its mucolytic action on intracellular mucus is not known.

Sammons[10] presented evidence indicating that the source of lysozyme in the feces in ulcerative colitis may be the pus cells. This would oppose the possibility of an etiological role. He found a second mucinase in the feces of patients with ulcerative colitis not present in normal persons, which, unlike lysozyme, does attack mucus. He suggests that this mucinase may play a part in the etiology of ulcerative colitis.

Lysozyme has not been generally accepted as a causative agent of ulcerative colitis. It is, however, being more widely studied as an index of the degree of activity of the disease process and as a measure of the available functioning colonic tissue. Further research in this field should produce results of much clinical importance.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

During much of the first century of its life your American Medical Association was concerned primarily with purely scientific affairs. Socioeconomic pressures on medicine, however, began piling up during the depression and the war. They were accompanied by and, in part, caused by increasing governmental ventures into health and medical care. The government also wielded an indirect influence on American medicine as we had known it by great increases in taxation, which destroyed much of the private support for our hospitals and medical schools.

These socioeconomic pressures created new problems and duties for your national Association. It became necessary to establish new departments to deal with them. In 1943 the House of Delegates created one of the most important of these—the Council on Medical Service and Public Relations. Its purpose was to "study the effect of social and economic changes on the practice of medicine and to report these changes to the profession."

This Council indeed has been a pioneering one. It has had to steer a path through turbulent and uncharted waters. Some of its early projects expanded so greatly and became so important that they were separated from the Council and set up as separate departments directly under the Board of Trustees. The two outstanding examples of this are the Washington Office and the Department of Public Relations.

Today the Council, known by the shortened title "Council on Medical Service," works in seven major areas. It has a committee to conduct studies and develop long-range plans in each. The seven areas are (1) prepayment hospital and medical service, (2) relations with lay-sponsored voluntary health plans, (3) federal medical services, (4) extension of hospitals and other facilities, (5) maternal and child care, (6) indigent care, and (7) medical care for industrial workers. I shall be able to touch only briefly on the Council activities in these fields. To do justice to them, a President's Page would have to be written about each committee.

The Council's Committee on Prepayment Hospital and Medical Service studies and evaluates voluntary health insurance plans, both those written by private insurance carriers and those sponsored by medical societies. It accepts applications for the Council's Seal of Approval and grants it to those plans meeting Council standards. The Committee also studies ways and means of improving benefits under all types of voluntary health insurance.

With the growth in recent years of a number of lay-sponsored and lay-managed health insurance plans, the Council set up a special committee to establish criteria for evaluating such plans. This Committee maintains liaison with the managing groups and is encouraging them to establish high standards of health service.

The Committee on Federal Medical Services was originally called the Committee on Medical Care for Veterans, and its early work was confined to the study of the several medical programs of the Veterans Administration. Its work has now been broadened to include the study of all federal activities in the medical care field not covered by other A. M. A. Councils or committees. (For example, the Council on National Emergency Medical Service handles relations with the Civil Defense Administration and the Medical Services of the Armed Forces.)

One of the most active committees is that on the Extension of Hospitals and Other Facilities. It considers hospital-physician relationships and encourages state and county medical societies to set up liaison committees between hospitals and physicians. It follows progress made under the Hill-Burton Hospital Construction Act. It advises on the development of needed health centers, diagnostic clinics, and outpatient dispensaries. Quite naturally, one of its activities is to study the distribution of physicians and to attempt to improve the situation in areas short of doctors. Accordingly, it operates the A. M. A.'s National Placement Service, which serves communities needing a physician and physicians seeking a place to practice.

The Committee on Maternal and Child Care regularly reviews activities in that field. It reports its findings to the profession, and, from the information gathered, is developing suggested minimal programs for communities of various sizes. Because of the recent agitation in governmental circles for a revival of the Emergency Maternal and Infant Care program, the Committee is currently conducting a series of studies to determine whether an emergency program is necessary.

Another Committee that is currently conducting a series of studies is the Committee on Indigent Care. These studies, which have been under way for the past year, cover all the various types of indigent care programs in operation in the United States. From the findings the Committee hopes to determine trends in indigent care and will attempt to formulate some suggested programs. One trend that the Committee has noted is the increasing amount of public assistance medical care being rendered by local health departments. The Committee endeavors to determine the relationship of the private practitioner to such programs as well as to all other indigent care plans.

Working closely with the Council on Industrial Health, the Committee on Medical Care for Industrial Workers reviews the scope of medical care programs now available to industrial workers. It also evaluates the status of physicians in industrial medical care programs. The Committee has given special attention to a study of cash sickness benefits legislation.

As is clear from the above description, much of the work of the Council on Medical Service is in the nature of surveys, studies, and evaluations. The material developed by its various committees is available to members of the A. M. A. who are faced with similar problems in their local communities. In addition to coordinating the activities of its Committees, the Council is concerned with many other problems and programs such as group practice, emergency medical call programs, health councils, temporary disability benefits, grievance committees, social insurance programs in foreign countries, local health units, multiphasic screening, and union health programs. Loan packets are available on these subjects as well as on some of the Committee activities. The Council can supply information on voluntary health insurance and on socialized medicine.

With socioeconomic problems ever present, we hope you will call upon your A. M. A.'s Council on Medical Service for the information it has available. It has been compiled as a service to members of the American Medical Association.

JOHN W. CLINE, M.D., San Francisco.

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ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Female Military Medical Officers

Senator Hunt of Wyoming introduced S. 2552, and Representative Durham of North Carolina introduced H. R. 6288. These bills are identical and would authorize the appointment of qualified women as physicians and specialists in the medical services of the Army, Navy, and Air Force. The bills would authorize the commissioning of women as officers to perform medical, dental, or medical service duties in the armed forces with equal rank and responsibility as now designated for male officers. These bills are similar to H. R. 4384 of the last Congress, which passed both the House and Senate. While these bills were being considered by a conference committee, the Congress adjourned, thus preventing their enactment.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. 156, proposes the creation of a **state board of medical herbalists** and defines a medical herbalist as a college graduate who holds a diploma from a recognized medical herbalist college, has studied anatomy, physiology, materia medica, toxicology, pharmacology, the metric system of weights and measures, diagnosis of diseases and herbal treatments for various diseases and malfunctioning conditions of the human body, and who deals exclusively in herbs, roots, barks and the compounding, preparation, and administration of the same as herbal remedies in the form of infusion, decoction, fermentation in substance, solid and fluid extracts, and tinctures and other natural forms. H. 161, proposes that no medicinal preparation or appliance having special utility for the prevention of **venereal disease** shall be sold except by an establishment holding a state license therefor issued by the state board of pharmacy except that the proposal would not apply to a duly licensed physician in the regular course of his practice. H. 162, proposes the creation of an **Arizona board of medical technology** which is defined to mean a science, art or technic of performing laboratory tests or examination on, or of, the blood, blood serum, feces, urine, sputum, exudates, transudates, organ contents or by-products thereof, from the human body, living or deceased, the results of which are used or interpreted by a practitioner licensed to engage in the practice of medicine. H. 168, to amend the law relating to **naturopathy**, proposes that approved colleges shall include in their course of study training in minor surgery, biochemistry, and phytotherapy in addition to subjects already covered by the law. The proposal would also add to the naturopathic act conditions under which it may be possible for licentiates to practice minor surgery after demonstrating proof of additional educational qualifications and passing a special examination.

Colorado

Bill Introduced.—H 76, proposes the creation of a committee on mental hygiene to make a survey and study of **mental health problems** of the state.

Bill Enacted.—S. J. R. 12, was adopted Feb. 8, 1952, it creates a legislative committee to investigate the feasibility of establishing additional public facilities for the **care of the aged** either by enlargement of the Colorado State Hospital or by the establishment of one additional institution or several small institutions at various points throughout the state.

Kentucky

Bills Introduced.—H. 155, proposes that any person who has been engaged in the **practice of medicine for forty years** prior to the effective date of this act and who presents affidavits from two reputable licensed members of the medical profession who practice in the same general locality with him and know his professional qualifications to the effect that he is qualified to be a member of the medical profession shall be entitled to a license to practice medicine upon application to the state board of health. H. 172, proposes to require the department of health to establish and maintain services and facilities, including hospital schools, for the care and education of **physically handicapped persons** and to provide in connection therewith medical and nursing care. H. 174, proposes the creation of an **alcoholic study commission** to make a comprehensive study of the problem of alcoholism in the state, the existing methods and facilities for treatment, the present program of public education on alcoholism, and the present status of the laws of the state in regard to alcoholism. H. 280, proposes that no person engaged in any of the healing arts shall employ **the title Doctor** unless he actually has graduated and holds a Doctor degree from a school, college, university, or institution authorized by its governing body to confer such degree. In such instances the person using the title Doctor must designate the particular Doctor degree which he holds. S. 93, proposes that no dog license shall be issued to any person unless he presents a certificate from a licensed veterinarian indicating that the dog has been **immunized against rabies or hydrophobia** within the preceeding twelve months.

Maryland

Bills Introduced.—S. 5, to amend the law relating to **narcotic drugs,** proposes to include the drugs, isonipecaine, amidone and dromoran within the definition of "narcotic drugs" together with synthetic drugs having comparable habit-forming qualities. S. 19, to amend the law relating to **rabies,** proposes that when a dog subject to rabies has bitten any person it shall be the duty of any person having a knowledge of such fact to report the same to the county health officer who shall see that such dog is confined for such period of time as the health officer shall direct.

Massachusetts

Bill Introduced.—S. 482, proposes that after **medical examiners and associate medical examiners** have completed a seven year term they shall, if reappointed, hold their offices during good behavior. At the time of being reappointed they shall show aptitude for the work and be certified by an accredited medical college as having done graduate study in medico-legal investigation under qualified authority.

Michigan

Bills Introduced.—H. 286, proposes to authorize the board of supervisors of counties having a population of over 500,000 to **abolish the office of coroner** and create the office of county medical examiner. S. 240, proposes regulations for the **licensing of trained certified graduate professional nurses,** practical nurses, and trained attendants.

New Jersey

Bills Introduced.—A. 265, proposes to prohibit the sale of any drug or medicinal preparation or appliance intended to prevent the spread of **venereal disease** except by duly licensed practitioners of medicine or in pharmacies or drug stores, for whose operation a permit has been duly issued by the board of pharmacy. A. 288, to amend the workmen's compensation law, proposes among other things that an injured employee may, when care is required, **select** to treat him any **duly licensed physician** and proposes that if the employee is unable to do so, or elects not to do so, the employer shall promptly provide him with the necessary medical care.

Rhode Island

Bills Introduced.—H. 586, proposes to make it an obligation of the state to provide state paid hospital and medical services for all state employees. H. 605, proposes the creation of a special commission to make an intensive study of the state laws relating to **narcotics.** H. 636, proposes the creation of a special commission to make a complete study of the Rhode Island **temporary disability insurance act.**

Virginia

Bills Introduced.—S. 196, proposes to prohibit the sale of drugs, medicines and appliances for the prevention of **venereal disease** except by duly licensed practitioners of medicine or in pharmacies and retail stores which have obtained a permit from the state board of pharmacy. S. 227, to amend the medical practice act, proposes regulations authorizing the licensure of persons who graduate from **foreign medical schools.** S. 278, to amend the medical practice act, proposes to authorize persons who are **interning or taking residency training** within the state to extend the three-year period of training for two additional years before being required to obtain a license to practice medicine.

APPOINT FIELD DIRECTOR FOR COUNCIL ON RURAL HEALTH

Mr. Aubrey D. Gates has been appointed to the permanent staff of the Council on Rural Health to serve as Field Director, effective Feb. 1. The Council on Rural Health hopes that the state medical societies and the state committees on rural health will take full advantage of Mr. Gates' services whenever possible. His headquarter's address will be 1801 N. Polk St., Little Rock, Ark. In making the announcement, Dr. F. S. Crockett, Chairman of the Council, said "It is our intent to have Mr. Gates spend practically all of his time in the field. He will want to contact the headquarters offices of the state medical societies, the extension workers in the state land-grant agricultural colleges, leaders in agriculture and other organizations interested in the program of rural health."

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

MEDICAL NEWS

ALABAMA

Annual Stuart Graves Lecture.—Dr. Alton Ochsner, Henderson Professor of Surgery and head of the department of the Tulane University of Louisiana School of Medicine, New Orleans, will deliver the annual Stuart Graves Memorial Lecture of the Nu Sigma Nu medical fraternity at the Medical College of Alabama, Birmingham, on March 18.

Public Health Institute.—The Dental Service of the Veterans Administration Hospital at Tuskegee will present an Institute of Public Health in the auditorium of Tuskegee Institute March 16-19. Collaborating agencies include the state departments of public health, welfare, and vocational rehabilitation, the Tennessee Department of Public Health, various groups associated with Tuskegee Institute, the U. S. Public Health Service and Department of Agriculture, and the University of Alabama. About 40 speakers will participate in the program.

COLORADO

Personals.—Dr. Joseph E. Cannon, Providence, R. I., has been appointed chief of the tuberculosis section of the state health department.——Dr. John D. Gillaspie has been named mayor of Boulder by the city council, while Dr. James E. Donnelly was accorded a similar honor at Trinidad.

Health Broadcasts for School Children.—The Colorado State Medical Society's popular mystery-drama series, "Dr. Tim, Detective," is being released the week of Feb. 24. It will be carried by 13 stations and will be broadcast weekly for 13 weeks. Designed for school youngsters in the sixth, seventh, and eighth grades, "Dr. Tim" is also popular with other age groups and with parents. Again this year it has strong support from school officials, women's clubs, Parent Teachers Association groups, and from the medical profession and the woman's auxiliaries. "Dr. Tim" won a national award in 1950 at Ohio State University's Institute of Education Through Radio.

CALIFORNIA

Colver Research Foundation.—A dinner in honor of Dr. Benton Noble Colver, for many years head of the department of otolaryngology, College of Medical Evangelists, Loma Linda-Los Angeles, was given at the Biltmore Hotel in Los Angeles, Jan. 20. The heads of the teaching department of the college and a large number of otolaryngologists of Southern California were present. On this occasion the Colver Research Foundation was inaugurated. It was formed by subscriptions and gifts of former students, associates, and hosts of friends to stimulate research in otorhinolaryngology.

CONNECTICUT

Rickettsialpox.—Dr. James C. Hart, Connecticut Department of Health, has reported a localized outbreak of rickettsialpox, which occurred among occupants of an apartment house. These are the first cases to be reported in Connecticut. Large numbers of house mice, *Mus musculus*, and mites, *Allodermanyssus sanguineus Hirst*, were found in the apartment house.

Annual County Society Conference.—The Connecticut State Medical Society will sponsor its annual conference for county medical association officers March 20 in New Haven. The program will include talks and discussions on membership services, professional relations with hospitals, medical public relations, and the program of the American Medical Education Foundation.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

GEORGIA

Medical Assembly and Surgical Congress.—The Atlanta Graduate Medical Assembly of the Fulton County Medical Society will be held in the New Auditorium of the Biltmore Hotel, Atlanta, March 10-13. The Southeastern Surgical Congress will meet in the Georgian Ball Room at the Biltmore on the same dates. Out-of-state speakers and their subjects for the graduate assembly include:

Edward H. Rynearson, Rochester, Minn., Is Obesity an Endocrine Problem?
George E. Shambaugh Jr., Chicago, Management of Deafness.
Hugh McCulloch, Chicago, Rheumatic Fever and Rheumatic Heart Disease.
George E. Burch, New Orleans, Diseases of the Heart. Diseases of the Kidney.
Edward G. Waters, Jersey City, Arterial Ligation for Post Partum Hemorrhage.
John L. Emmett, Rochester, Minn., Therapy in Genitourinary Tuberculosis.
Nicholson J. Eastman, Baltimore, subject to be announced.
Shields Warren, Boston, Acute Radiation Syndrome.
Cornelius P. Rhoads, New York, Clinical Endocrinology and the Cancer Problem.
Francis D. Moore, Boston, Metabolic Response to Surgery and Injury, Modern Treatment of Burns.
Joe V. Meigs, Boston, subject to be announced.
Albert M. Snell, Palo Alto, Calif., subject to be announced.

There will be a symposium on diseases of the liver on Monday, a symposium on cardiac and hypertensive states on Tuesday, and another on gastroenterology on Wednesday.

Out-of-section speakers of the surgical congress include:

John deJ. Pemberton, Rochester, Minn., Carcinoma of the Thyroid.
Claude S. Beck, Cleveland, Operation for Coronary Occlusion.
George Crile Jr., Cleveland, Surgical Treatment of Ulcerative Colitis.

One registration fee of $15 will admit a physician to both assemblies.

INDIANA

Medical-Civic Dinner.—The Vanderburgh County Medical Society will hold its first annual medical-civic dinner March 4 in the Rose Room of the Hotel McCurdy in Evansville. Certificates of appreciation will be awarded to all living past presidents of the society. About 100 leading business and civic leaders will be guests. Frank Sparks, president of Wabash College, Crawfordsville, will be the principal speaker.

KANSAS

Annual Porter Lectures.—Dr. Otto Loewi, research professor, department of pharmacy, New York University College of Medicine, will deliver the 19th annual Porter Lectures at the Kansas University Medical Center and on the Lawrence campus. At 4 p. m. on March 31 at the university, he will speak on "Problems in the Field of Adrenal Function." On April 1 at 11 a. m. in Strong Hall on the Lawrence campus, his subject will be "From the Workshop of Discoveries." He will speak on "Mechanism of Drug Action" at the medical center April 1 at 4 p. m. In addition, Dr. Loewi will address the medical students in Kansas City Monday noon March 31 on "Reflections on the Study of Medicine." Funds for the Porter Lectures were provided by a bequest of the late Dr. J. L. Porter of Paola, Kans.

KENTUCKY

Retiring Physician Honored.—Dr. Alice N. Pickett, head of the obstetrics department of the University of Louisville School of Medicine for 25 years and professor emeritus for 5 years, was honored by a testimonial dinner at the Brown Hotel, Louisville, Jan. 28, by the Louisville Obstetrical and Gynecological Society. A silver dish was presented her by the society on her retirement as an obstetrician.

Personal.—Dr. Joseph A. Little, Louisville pediatrician, has been named to serve as medical director of the Kentucky Crippled Children's Commission on a part time basis by contract between the commission and the University of Louisville School

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of Medicine. He will supervise the medical programs of the commission at Kosair Crippled Children Hospital in Louisville, and Cardinal Hill Convalescent Hospital in Lexington, as well as programs in Covington, Ashland, Owensboro, and Paducah.

LOUISIANA

Psychosomatic Problems in Children.—The first meeting of the Psychosomatic Forum of New Orleans will be held at 8:30 p. m. Feb. 28 in the board room of the Orleans Parish Medical Society, New Orleans. Papers on psychosomatic problems in children will be given by Drs. Irwin M. Marcus, Ian Stevenson, and Clifford G. Grulee Jr., all of New Orleans. The subjects covered will include enuresis, diabetes, and infantile colic. Drs. Ralph V. Platou and Myron E. Wegman, New Orleans, will participate with the speakers in a panel discussion following presentation of the papers.

MARYLAND

New State Medical Journal.—The *Maryland State Medical Journal* began publication with the January issue. It will report the activities of the Medical and Chirurgical Faculty of the State of Maryland, its publisher, incorporating the faculty's former *Bulletin* and *Newsletter*. The editor is Dr. George H. Yeager, Baltimore. The faculty has had other official publications. From October, 1839, to June, 1843, it published the *Maryland Medical and Surgical Journal and Official Organ of the Medical Department of the Army and Navy of the United States*. From May, 1887, to March, 1918, a publication known as the *Maryland Medical Journal* carried the notes and communications of the faculty. For a brief period, 1905-1908, it became the official publication medium of the faculty and included transactions. In 1908 the house of delegates terminated its contract with the *Maryland Medical Journal* and initiated an official monthly *Bulletin*, which was discontinued in 1922. The new journal is similar in format to other state medical journals issued by state medical associations. It is a member of the State Journal Advertising Bureau.

MASSACHUSETTS

Personal.—Dr. William C. Moloney, clinical professor of medicine, Tufts College Medical School, and assistant director of the first and third (Tufts) Medical Services at the Boston City Hospital, will leave Boston with his family for Hiroshima, Japan, April 1. He will serve for the next two years as internist with field units of the Atomic Bomb Casualty Commission, which are engaged in the study of the effects of atomic radiation in Hiroshima and Nagasaki. This work is under the direction of the National Research Council and the National Academy of Science.

Bay State Rehabilitation Conference.—The second annual Bay State Rehabilitation Conference will be held March 12 at the Copley Plaza Hotel, Boston. The morning discussion will center around manpower and rehabilitation and what can be done to encourage employment of the handicapped. Harry E. Howard, personnel manager at the Norton Company, Worcester, will be chairman. The afternoon subject will be "Helping Them to Help Themselves." A clinical demonstration will be introduced by Dr. Joseph S. Barr, chief of orthopedic service at Massachusetts General Hospital. Cases will be presented and discussed by Drs. Henry H. Kessler, West Orange, N. J.; Elmer F. Franseen, Springfield; Robert C. Hartson, Worcester; William E. Kenney, Fall River, and Arthur L. Watkins, Boston.

MICHIGAN

Ford Hospital Appointments.—Dr. Lawrence S. Fallis has been appointed surgeon-in-chief and Dr. John G. Mateer, physician-in-chief at Henry Ford Hospital, Detroit. Dr. Fallis, who succeeds the late Dr. Roy D. McClure, has been on the staff of the hospital since 1925. Dr. Mateer succeeds Dr. Frank J. Sladen, who retired Feb. 1 as head of the department of medicine, a post he had held since the hospital was organized by the late Henry Ford in 1915. Dr. Mateer joined the staff of the hospital in charge of the division of gastroenterology in 1920.

NEW YORK

Roswell Park Medal.—On Feb. 14 the Buffalo Surgical Society presented the fifth Roswell Park Memorial Medal for "outstanding surgical achievement" to Dr. Edward D. Churchill of Boston. He delivered the annual Roswell Park Lecture entitled "The Architectural Basis of Pulmonary Ventilation."

Postgraduate Instruction.—Three postgraduate lectures have been arranged for the Rensselaer County Medical Society to be given in Troy Tuesday evenings at 8:30 p. m. as follows:

March 11, Samaritan Hospital, Leon G. Berman, Syracuse, Diagnosis and Treatment of the Acute Surgical Abdomen.
April 8, Leonard Hospital, Marvin Stern, Brooklyn, Recognition and Management of Psychiatric Problems in General Practice.
May 6, St. Mary's Hospital, Emil Granet, New York, Recent Progress in the Management of Common Anorectal Lesions.

This instruction has been arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health.

New York City

Annual Elsberg Lecture.—Dr. Gilbert Horrax, Boston, will deliver the annual Charles A. Elsberg Lecture of the New York Society of Neurosurgery March 18 at 8:30 p. m. in the New York Academy of Medicine Building. His subject will be "The Development of Brain Tumor Surgery." Dr. Horrax is neurosurgeon to the New England Deaconess and New England Baptist hospitals, Boston.

Mount Sinai Hospital Centennial.—Mount Sinai Hospital on Jan. 16 opened the year long observance of its 100th anniversary. The year will be marked by an historical exhibit, a symposium on medicine and society, publication of the history of the hospital, and dedication of the hospital's first maternity pavillion and two new laboratory buildings. The hospital had its first home in a four-story building with a 45 bed capacity. It was incorporated on Jan. 16, 1852, as the first Jewish sponsored hospital in the United States, and opened its doors to the first patient in May, 1855. In its first year the hospital treated 225 patients at a cost of $5,493. Today it treats 40,000 a year and its annual operating cost is $5,500,000.

NORTH CAROLINA

Narcotic Violations.—Dr. Marvin A. Bowers, Winston-Salem, pleaded *nolo contendere* in the United States District Court at Winston-Salem, and has been placed on probation for a period of five years and fined $1,000.——Dr. Robert H. Freeman, Raleigh, pleaded guilty to a violation of the federal narcotic law and on Dec. 13, 1951, was sentenced to a term of three years.

OHIO

Personal.—Dr. Elmore R. McNeal, Youngstown, has been appointed editor of the *Mahoning County Medical Society Bulletin*, succeeding Dr. Stephen W. Ondash, Youngstown, who will continue to serve as one of the associate editors.

Academy Members Awarded Fifty-Year Pins.—The Cincinnati Academy of Medicine in December honored 13 members. The 9 physicians who were presented 50 year membership pins are Drs. Martin H. Fischer, Tilden J. Beck, George S. Buttemiller, Thomas Hulick, William E. Leever, Francis M. Oxley, Frederick C. Theiss, Harry J. Wittenberg, and Henry L. Woodward. Pins were presented to members of the families of Drs. John P. Beneke, William L. Brodberger, George A. Pierret, and Joseph S. Podesta. At the scientific session Dr. Alan R. Moritz, professor of pathology at Western Reserve University, Cleveland, spoke on problems of crime detection.

OKLAHOMA

General Practitioners Meeting.—The second annual meeting of the Oklahoma Academy of General Practice will be held at the Tulsa Hotel March 16-18. The scientific program beginning on Monday includes a seminar on juvenile delinquency with Dr. Stanley R. Truman, Oakland, Calif., as moderator and Dr. Edward D. Greenwood, Topeka, Kan., Dr. Paul C. Benton, Miss Elba L. Dyer, and Mr. Howard M. Scott, all of Tulsa, and

answer period will close the afternoon program with Dr. Harry Gold of New York serving as moderator. Lectures on orthopedics and orthopedic problems will be given Thursday. The banquet speaker Wednesday evening will be Kenneth McFarland of Topeka, Kan., educational director for American Trucking Associations, Inc., and educational consultant for General Motors. Scientific exhibits will be keyed to each lecture subject. Many of the 179 firms in the technical exhibit will also relate their exhibits to the scientific program.

FOREIGN

British Congress of Obstetrics and Gynecology.—This congress will be held July 8-11 at the University of Leeds, England, under the presidency of Prof. Andrew Claye. The first paper will be by the guest speaker Prof. M. A. Bastiaanse of Holland, on "Cancer of the Body of the Uterus." Other papers to be presented include:

Abnormal Uterine Action During Labor, G. H. Bell, Dundee, W. C. W. Nixon, London.
Place of the Pediatrician in a Maternity Unit, W. Gaisford, Manchester, Mr. F. Stabler, Newcastle.
Stress Incontinence of Urine, A. H. Aldridge, New York, T. N. A. Jeffcoate, Liverpool.
Genital Tuberculosis in the Female, Magnus Haines, London, Mr. John Stallworthy, Oxford.

Membership forms may be secured through one of the secretaries, Brian Jeaffreson, The Hospital for Women, Coventry Place, Leeds.

DEATHS IN OTHER COUNTRIES

Professor Henri Hartmann, Paris, for 32 years professor in the French Faculty of Medicine, died January 3, aged 91, of a heart attack, according to the *New York Times*. He was one of the two founders in 1918, and a former president of the French League Against Cancer, and a former president of the French Academy of Medicine. He was president of the Association for the Development of Medical Relations between France and other countries and a Grand Officer of the Legion of Honor. During World War I he performed many operations on wounded soldiers in Paris hospitals.——**Frederick Murgatroyd,** Ch.B., who was appointed a little over a year ago to the Wellcome Chair of Clinical Tropical Medicine at the University of London, died December 16. Dr. Murgatroyd had been on the faculty of the Liverpool School of Tropical Medicine from 1927-1937, when he joined the School of Hygiene and Tropical Medicine in London as a lecturer.

MEETINGS

AERO MEDICAL ASSOCIATION, Washington, D. C., March 17-19. Dr. Thomas H. Sutherland, 214 South State St., Marion, Ohio, Secretary.
ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.
AMERICAN ACADEMY OF FORENSIC SCIENCES, Biltmore Hotel, Atlanta, Ga., March 6-8. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.
AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.
AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.
AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.
AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.
AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.
AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.
Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.
Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.
AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116 South Michigan Ave., Chicago 3, Secretary.
AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. Dr. Willian H. Bunn, 1775 Broadway, New York 19, Secretary.
AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., Feb. 25-27. Dr. Nina Ridenour, 25 West 54th St., New York 19, Secretary.
AMERICAN PSYCHOSOMATIC SOCIETY, Chicago, March 29-30. Dr. Frederick C. Redlich, 551 Madison Avenue, New York 22, Secretary.
AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New York, April 14-18. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.
AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Dr. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.
AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W Va., Apr. 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.
CENTRAL SURGICAL ASSOCIATION, Toronto, Can., March 6-8. Dr. James T. Priestley, 102 Second Avenue S.W., Rochester, Minn., Secretary.
CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, March 4-7. Dr. Walter C. Bornemeier, 86 East Randolph St., Chicago 1, Secretary.
JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.
MICHIGAN CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 12-14. Dr. E. F. Sladek, 123 E. Front St., Traverse City, Chairman.
MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.
NATIONAL CONFERENCE ON RURAL HEALTH, Shirley-Savoy Hotel, Denver, Feb. 28-Mar. 1. Dr. F. S. Crockett, 535 North Dearborn St., Chicago 10, Chairman.
NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 10-13. Dr. Woodward D. Beacham, 1430 Tulane Ave., Room 105, New Orleans 12, Secretary.
NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 22. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.
PACIFIC COAST SURGICAL ASSOCIATION, Del Monte, Calif., Feb. 26-29. Dr. Carleton Mathewson Jr., Stanford University Hospital, San Francisco, Secretary.
PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.
POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.
SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., March 21-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.
SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.
SOUTHEASTERN SURGICAL CONGRESS, Atlanta, Ga., March 10-13. Dr. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.
SOUTHWEST ALLERGY FORUM, Hotel Baker, Dallas, Texas, March 2-4 Dr. James Holman, Medical Arts Bldg., Dallas, Secretary.
TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.
UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Monterrey, Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. Court House, El Paso, Texas, Secretary.
WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Del Monte Lodge, Pebble Beach, Calif., March 2-3. Dr. Nicholas A. Bercel, 450 North Bedford Drive, Beverly Hills, Calif., Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.
COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.
CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.
EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.
EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.
INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.
INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.
INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.
INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.
INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

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INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV°, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF LEGAL AND SOCIAL MEDICINE, Berne, Switzerland, April 15-18. Prof. J. Dettling, 20, Buhlstrasse, Berne, Switzerland.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Panama City, R. P., Feb. 24-29. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York, N. Y., U. S. A., Executive Director.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 24-26, 1952. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ALASKA:* *Examination.* Juneau, March 4. Also on application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA:* *Examination.* Phoenix, April 15-17. *Reciprocity.* Phoenix, April 19. Sec., Dr. J. H. Patterson, 316 W. McDowell St., Phoenix.

ARKANSAS:* *Examination. Regular.* Little Rock, June 5-6. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic.* Little Rock, June 10-11. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 5-6. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: *Written.* Los Angeles, Feb. 18-21; San Francisco, June 23-26; Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* San Francisco, June 21; Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 22; Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO:* *Examination.* Denver, June 10-12. Final date for filing application is May 12. *Reciprocity.* Denver, April 8. Final date for filing application is Mar. 10. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

CONNECTICUT:* *Regular Examination.* Hartford, March 11-12. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic Examination.* Derby, March 11. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA:* *Reciprocity.* Washington, March 10. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA:* *Examination.* Jacksonville, June 29-July 1. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta and Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capital, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

IDAHO: Boise, July 14-16. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLIONOS: *Examination.* Chicago, April 1-3, June 24-26 and Oct. 7-9. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 1952. Sec., Dr. Paul R. Tindall, 1138 K of P Bldg., Indianapolis 4.

IOWA:* *Examination.* Iowa City, June 9-11. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 4-5. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 4-6. Sec., Dr. Bruce Underwood, 620 S. Third St., Louisville.

MAINE: Portland, March 11-12. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 17-20. Sec., Dr. Lewis P. Grundy, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 17-18. Sec., Dr. John A. Evans, 6029 Belliona Ave., Baltimore.

MICHIGAN:* *Examination.* June. Sec., Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MINNESOTA: Minneapolis, April 15-17. Sec., Dr. Julian F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 1. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEW HAMPSHIRE: Concord, March 12-13. Sec., Dr. John S. Wheeler, State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO:* Santa Fe, April 14-15. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Pinehurst, May 5. *Written.* Raleigh, June 16-19; *Reciprocity.* Raleigh, June 17. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 17-20. *Reciprocity.* Columbus, April 1. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 4-5. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Reciprocity.* Portland, April 18-19. *Examination.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PUERTO RICO: *Examination.* San Juan, March 4. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

RHODE ISLAND:* *Examination.* Providence, April 3-4. Sec., Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Reciprocity.* Columbia, March 3 and April 7. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Rapid City, July 15. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TENNESSEE:* *Examination.* Memphis, March 26-27. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Fort Worth, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 314 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

VIRGIN ISLANDS: St. Thomas, June 4-5. Sec., Dr. Earle M. Rice, St. Thomas.

WEST VIRGINIA: Charleston, April 7-8. Sec., Dr. H. H. Dyer, State Office Bldg. No. 3, Charleston 5.

WASHINGTON: Seattle, July. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WISCONSIN:* Milwaukee, July 8-10. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: Tucson, March 18. Sec., Mr. Herbert D. Rhodes, University of Arizona, Tucson.

COLORADO: Denver, March 5-6. *Examination.* Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 21-22. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington, D. C.

FLORIDA: Gainesville, June 7. *Examination.* Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

OKLAHOMA: *Examination.* Oklahoma City, April 14. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 1, June 7, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

TENNESSEE: *Examination.* Memphis and Nashville, March 20-21. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

TEXAS: Austin, April. *Examination.* Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 5, and Milwaukee, June 7. Sec., Mr. W. H. Barber, Ripon College, Ripon.

* Basic Science Certificate required.

DEATHS

Blake, Francis Gilman ✙ New Haven, Conn., Sterling Professor of Medicine, Yale University School of Medicine, died in Walter Reed General Hospital, Washington, D. C., Feb. 1, aged 64. Dr. Blake was born in Mansfield Valley, Pa., Feb. 22, 1887. He graduated from Dartmouth College, Hanover, N. H., in 1908 and received his medical degree from Harvard Medical School, Boston, in 1913. For the next three years he was on the staff of Peter Bent Brigham Hospital in Boston as intern, assistant resident, and resident physician. In 1916 he went to the Rockefeller Institute for Medical Research for a year. From 1917 to 1919 he was assistant professor of medicine at the University of Minnesota Medical School, Minneapolis. In 1919 he returned to the Rockefeller Hospital in New York as associate in medicine, in 1920 became an associate member of the Rockefeller Institute, and from 1924 to 1935 was a member of its scientific board of directors. At the time of his appointment to the Yale University School of Medicine faculty in 1921 he was the youngest man ever to be named to a full professorship there. He was John Slade Ely Professor of Medicine from 1921 to 1927, when he became Sterling Professor of Medicine, a post he held at the time of his death. He served as dean from 1940 to 1947 and in the latter year resigned that position to devote his full time to the chairmanship of the department of internal medicine and to his work for various governmental and scientific agencies. Since Jan. 1 of this year, as civilian technical director of medical research in the office of the Army Surgeon General, Dr. Blake had served as expert consultant to the chairman of the Army Medical Research and Development Board in the evaluation of current and proposed research projects conducted by Army medical installations and 81 cooperating civilian institutions. On leave of absence from Yale, Dr. Blake retired earlier this year as chairman of the Committee on Medical Sciences of the Research and Development Board in the Office of the Secretary of Defense. He had held that post since 1948. During World War I Dr. Blake rose to the rank of major in the medical reserve corps of the U. S. Army. During World War II he served as special consultant to President Roosevelt and Secretary of War Stimson and as president of the Army Epidemiological Board. For his work as director of the Field Commission on scrub typhus in New Guinea in 1943, he received the United States Typhus Medal and in 1944 he was awarded the Medal for Merit. From 1925 to 1936 he was a member of the National Research Council, Division of Medical Sciences, and chairman from 1933 to 1936; a member of the fellowship board from 1927 to 1946, chairman of the board from 1936 to 1946; a member of the committee on chemotherapy since 1940; a member of the clinical panel on antimalarials from 1942 to 1946 and of the medical committee since 1947, and chairman of the subcommittee on infectious diseases from 1940 to 1946. For many years he was a member of the National Advisory Health Council of the U. S. Public Health Service and chairman of the advisory council of the Life Insurance Medical Research Fund. In 1932 he was a member of the executive council of the Association of American Medical Colleges. He had been chairman of the Section on the Practice of Medicine of the American Medical Association in 1937-1938; past president and vice-president of the Association of American Physicians, of which he had been recorder from 1934 to 1940 and councilor from 1941 to 1947; past president of the American Society for Clinical Investigation and American Association of Immunologists; in 1946 vice-president of the American Association for the Advancement of Science; and a fellow, from 1939 to 1947 a regent, and in 1948 vice-president of the American College of Physicians. He was a fellow of the National Academy of Sciences, a member of the American Association of Pathologists and Bacteriologists, Society of American Bacteriologists, American Society for Experimental Biology and Medicine, American Society for Experimental Pathology, Connecticut Academy of Arts and Sciences, Harvey Society, Chi Phi, Phi Rho Sigma, Alpha Omega Alpha, and Sigma Xi. In 1939 he was a member of the executive committee of the Third International Congress of Microbiology. During the annual meeting of the Rhode Island Medical Society in 1945, Dr. Blake was awarded the Charles V. Chapin Memorial Award of the City of Providence and gave the annual Charles V. Chapin Oration before the medical society. In 1946 he received the Lasker Group Award for the Army Epidemiological Board. In 1935 he was a Harvey lecturer. Dr. Blake was certified by the American Board of Internal Medicine. Since 1921 he had been physician-in-chief of the Grace-New Haven Hospital, and was for many years vice-president of the board of scientific directors of the Yerkes Laboratories for Primate Biology. He had been prominently associated with many important developments in medical education and medical research and administration and has had a strong influence upon the modern growth of the Yale University School of Medicine. He had contributed through his research to the treatment of scarlet fever with antitoxin and to the treatment of pneumonia by serums and by sulfapyridine and its related compounds. Dr. Blake was the recipient of an honorary M.A. degree from Yale in 1921 and doctor of science degree from Dartmouth in 1936.

Trick, Harry Radley ✙ Buffalo; born in Stafford, N. Y., April 1, 1874; University of Buffalo School of Medicine, 1901; formerly on the faculty of his alma mater; member of the House of Delegates of the American Medical Association from 1929 to 1935; past president of the Medical Society of the State of New York; active in the Erie County Medical Society, serving as chairman of its committee for revision of the constitution and bylaws in 1934 and as a member of a similar committee in 1951; in 1920 and 1921 president of the medical alumni of the University of Buffalo; fellow of the American College of Surgeons and a former member of its board of governors; member of the Buffalo Surgical Society and Buffalo Academy of Medicine; for many years medical director of the Hospital Service Corporation of Western New York, known as Blue Cross; served during World War I; consulting surgeon, Wyoming County Community Hospital in Warsaw, Buffalo General, Edward J. Meyer Memorial, and Buffalo State hospitals; connected with an American Red Cross mobile unit of blood banks; died in Warren (Pa.) General Hospital Dec. 19, aged 77, of coronary artery disease.

Stucky, George Courtney ✙ Charlotte, Mich.; born in Louisville, Ky., May 10, 1888; University of Michigan Medical School, Ann Arbor, 1923; lecturer in public health practice, University of Michigan School of Public Health, Ann Arbor; certified by the American Board of Preventive Medicine and Public Health; served as president of the Michigan Health Officer's Association; past president of the Michigan Trudeau Society and Michigan Sanatorium Association; formerly a director of the National Tuberculosis Association; member of the American Trudeau Society and the American Public Health Association; served as a member of the board of trustees of the Michigan Tuberculosis Association; fellow of the American College of Physicians; director of the Eaton County Health Department; at one time associated with the W. K. Kellogg Foundation in Battle Creek; for many years superintendent and medical director of Ingham Sanatorium in Lansing; on the staff of the Hayes-Green-Beach Hospital, where he died Nov. 26, aged 63, of thrombosis of the basilar artery.

Black, Robert Alfred ✙ Chicago; born in Clarksburg, Pa., in April, 1879; Northwestern University Medical School, Chicago, 1904; professor emeritus of pediatrics at Stritch School of Medicine of Loyola University; specialist certified by the American Board of Pediatrics; past president of the Chicago Pediatrics Society and member of the board of governors of the Chicago Heart Association; member of the American Academy of Pediatrics; fellow of the American College of Physicians; at one time a member of the city board of health and acting president of the board late in 1938 and early in 1939; member of the advisory board of the Municipal Contagious Disease Hospital; retired head of the pediatrics service at Mercy Hospital; honorary chief

✙ Indicates Fellow of the American Medical Association.

of staff at La Rabida Jackson Park Sanitarium, where he had been on the visiting staff; served with St. Mary of Providence School for Handicapped Girls; died in Maitland, Fla., Jan. 13, aged 72, of pneumonia.

Aaron, Charles Dettie ✠ Detroit; born at Lockport, N. Y., May 8, 1866; University of Buffalo School of Medicine, 1891; from 1898 to 1938 professor of gastroenterology and dietetics at the Detroit College of Medicine, now a part of Wayne University College of Medicine, where he was an emeritus professor of gastroenterology; one of the founders, an honorary member, and, for many years, secretary-treasurer of the American Gastroenterological Association; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past president of the Detroit Academy of Medicine; author of "Diseases of Digestive Organs"; consultant in stomach diseases at Receiving and Shurly hospitals and Harper Hospital, where he died Dec. 3, aged 85, of arteriosclerosis.

Horan, Thomas Neil ✠ Detroit; born in Detroit April 3, 1902; University of Michigan Medical School, Ann Arbor, 1926; assistant professor of clinical medicine at Wayne University College of Medicine; certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served during World War II and was awarded the Bronze Star "for meritorious achievement in support of military operations"; on the staffs of Harper Hospital in Detroit and the Veterans Administration Hospital in Dearborn; in 1942 at the Atlantic City session of the American Medical Association was given honorable mention for his exhibit on laparoscopy, or intra-abdominal photography in color; died Dec. 1, aged 49, of myocardial infarction and arteriosclerotic heart disease.

Aldridge, Mahlon Roy ✠ Jefferson City, Mo.; St. Louis College of Physicians and Surgeons, 1907; died in St. Mary's Hospital Dec. 1, aged 73, of heart disease.

Allyr, Paul R. ✠ Waverly, Ill.; Barnes Medical College, St. Louis, 1903; city health officer; formerly mayor and member of the city council; died in Memorial Hospital, Springfield, Dec. 12, aged 72.

Arnold, Harold Sears, Woodbridge, Conn.; Yale University School of Medicine, New Haven, 1903; member of the American Medical Association; served on the faculty of his alma mater; affiliated with New Haven Hospital, where he died Dec. 20, aged 74, of pulmonary emphysema.

Baker, Frank Lawrence, Hildreth, Neb.; Lincoln Medical College of Cotner University, 1910; member of the board of education from 1930 to 1933; died in Holdrege Hospital in Holdrege Oct. 28, aged 66, of coronary artery disease.

Bender, Irwin Henry ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1923; on the staff of Samaritan Hospital; died in Long Island College Hospital Dec. 18, aged 52, of cerebral hemorrhage.

Beyer, Othmar Julius, Irvington, N. J.; Medizinische Fakultät der Universität, Wien, Austria, 1915; on the staff of Irvington General Hospital, where he died Dec. 3, aged 61, of coronary occlusion.

Boemer, Irving Henry ✠ St. Louis; St. Louis University School of Medicine, 1915; member of the International College of Surgeons; fellow of the American College of Surgeons; senior instructor in surgery at his alma mater; affiliated with St. John's Hospital, Missouri Pacific Hospital, and St. Mary's Group of Hospitals; died Dec. 3, aged 62, of cerebral infarction.

Brown, Edgar Milton, Zanesville, Ohio; Medical College of Ohio, Cincinnati, 1893; served during World War I; died in Good Samaritan Hospital Oct. 14, aged 85, of carcinoma of the kidney.

Brunner, Austin Franklin, Sharon Hill, Pa.; Jefferson Medical College of Philadelphia, 1931; member of the American Medical Association; served during World War II; president of the board of health of Sharon Hill; affiliated with Methodist Episcopal Hospital in Philadelphia and Taylor Hospital in Ridley Park; died Dec. 2, aged 44, of coronary occlusion.

Burke, Edward Francis ✠ Providence, R. I.; Tufts College Medical School, Boston, 1918; also a graduate in pharmacy; member of the New England Obstetrical and Gynecological Society; affiliated with Roger Williams General Hospital and St. Joseph's Hospital, where he died Dec. 20, aged 70, of carcinoma of the bladder.

Chidlow, Alexander D. ✠ Villa Park, Ill.; Jenner Medical College, Chicago, 1917; died in Du Page Memorial Hospital, Elmhurst, December 3, aged 72, of cerebral thrombosis.

Diefenderfer, Harold, Chicago; University of Pennsylvania Department of Medicine, Philadelphia, 1894; died Jan. 1, aged 82, of sclerotic myocarditis.

Dillon, John Alfred, Larned, Kan.; Kansas Medical College, Topeka, 1893; also a graduate in dentistry; member of the American Medical Association and in 1929 member of its House of Delegates; past president of the Kansas Medical Society; fellow of the American College of Surgeons; served as lecturer in psychiatry at the University of Kansas School of Medicine in Kansas City; superintendent of the Larned State Hospital from 1928 to 1945; died Dec. 3, aged 78, of cerebral hemorrhage.

Dittmer, Samuel Edward ✠ Kouts, Ind.; Hahnemann Medical College and Hospital, Chicago, 1911; served during World War I; physician and surgeon for the Erie Railroad; on the staff of Porter Memorial Hospital in Valparaiso, where he died Dec. 1, aged 66, of myocardial infarction.

Dougherty, James J., Avoca, Pa.; Jefferson Medical College of Philadelphia, 1908; member of the American Medical Association; served on the staffs of Taylor Hospital in Taylor, St. Mary's Hospital in Scranton, and Pittston (Pa.) Hospital; died Nov. 12, aged 70, of bronchopneumonia.

Fava, Philip Vincent, Newark, N. J.; Tufts College Medical School, Boston, 1924; fellow of the American College of Surgeons; attending gynecologist, Newark City Hospital; on the courtesy staffs of Presbyterian, St. James, Lutheran, and St. Michael's hospitals in Newark and St. Mary's Hospital in Orange; died Dec. 5, aged 54, of carcinoma of the transverse colon.

Fletcher, Benjamin Kennard, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1895; for many years professor of pediatrics at his alma mater; died in Hahnemann Hospital Dec. 17, aged 83, of carcinoma of the prostate.

Graves, Waldo Neil, Duluth, Minn.; Rush Medical College, Chicago, 1924; member of the American Medical Association; fellow of the American College of Surgeons; served during World Wars I and II; on the staffs of Miller Hospital, St. Mary's Hospital, and St. Luke's Hospital, where he died Dec. 5, aged 53, of carcinoma of the lung.

Handley, Walter Edward, Springfield, Mo.; Barnes Medical College, St. Louis, 1906; member of the American Medical Association; commissioner of health and sanitation; on the courtesy staff of Burge Hospital; died Nov. 26, aged 74, of acute coronary thrombosis.

Henderson, Edward Emmett ✠ Columbus, Kan.; University of Kansas School of Medicine, Kansas City, 1907; died Nov. 5, aged 84, of cerebral hemorrhage.

Hilborn, Robert Ross, Polkton, N. C.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1904; Cleveland Homeopathic Medical College, 1908; formerly a medical missionary in North Africa; died Nov. 14, aged 71.

Hughes, James Thomas, Fountain Run, Ky.; University of Tennessee Medical Department, Nashville, 1898; died Dec. 22, aged 77.

Jackson, Carl A. ✠ Kansas City, Mo.; University Medical College of Kansas City, 1897; an Associate Fellow of the American Medical Association; veteran of the Spanish-American War; on the staff of Trinity Lutheran Hospital, where he died Nov. 27, aged 74, of coronary occlusion.

Jacob, David, Springfield, Ill.; Universität Basel Medizinische Fakultät, Switzerland, 1936; member of the American Medical Association; served during World War II; died Oct. 3, aged 42, in an automobile accident.

Maloy, Daniel W. F., Milan, Ga.; Hospital Medical College, Atlanta, 1911; member of the American Medical Association; died Oct. 31, aged 61.

Montgomery, Enoch Albert, Unionville, Mo.; Barnes Medical College, St. Louis, 1899; member of the American Medical Association; past president of the North Central Counties Medical Society; died recently, aged 80, of carcinoma of the prostate.

Moore, Grover Cleveland ✙ Ponca City, Okla.; University of Arkansas School of Medicine, Little Rock, 1913; past president and secretary of Kay County Medical Society; on the staff of Ponca City Hospital; died Nov. 18, aged 64, of a heart disease.

Peters, William Chute, Bangor, Maine; born June 15, 1868; Tufts College Medical School, Boston, 1902; member of the American Medical Association and New England Surgical Society; fellow of the American College of Surgeons; past president of the Bangor Anti-Tuberculosis Association and the Maine Tuberculosis Association; served during World War I; at one time on the faculty of his alma mater as an assistant in microscopic anatomy and instructor in operative surgery; consulting surgeon, Eastern Maine General Hospital; died recently, aged 83.

Prince, Russell Warren ✙ San Bernardino, Calif.; California Eclectic Medical College, Los Angeles, 1916; on the staff of the San Bernardino Community Hospital; died Nov. 27, aged 60, of acute coronary thrombosis.

Radzow, Karl Herbert, Fontana, Calif.; Western Reserve University School of Medicine, Cleveland, 1943; member of the American Medical Association; interned at the City Hospital in Cleveland, where he subsequently held a residency in obstetrics and gynecology and was chief resident in obstetrics and gynecology; formerly resident in obstetrics and gynecology at the University Hospital in Cleveland; served during World War II; joined the staff of the Kaiser Fontana Hospital Association in July, 1950; killed Nov. 28, aged 34, in a car accident.

Roberts, Oscar Harvey, Bethel, Ky.; Kentucky School of Medicine, Louisville, 1898; died in Mount Sterling Nov. 6, aged 78, of uremia and carcinoma of the prostate.

Romig, Joseph Herman ✙ Colorado Springs, Colo.; Hahnemann Medical College and Hospital of Philadelphia, 1896; an ordained minister; fellow of the American College of Surgeons; member of the Alaska Territorial Medical Association; served for many years as medical missionary for the Moravian Missions of Alaska and at one time as mayor of Anchorage; died Nov. 23, aged 79.

Ross, Edward Smithers, Darby, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1920; died Nov. 19, aged 55.

Schmaltz, Walter Franklin, Dallas, Texas; Lincoln Medical College of Cotner University, 1910; specialist certified by the American Board of Otolaryngology; served during World War I; lieutenant colonel, retired, medical reserve corps, U. S. Army; formerly affiliated with the Veterans Administration hospitals in Waco and Dallas; died Oct. 15, aged 67, of paralysis agitans.

Schulz, Clarence Henry ✙ La Grange, Ind.; Indiana University School of Medicine, Indianapolis, 1926; on the staff of La Grange County Hospital; died November 17, aged 50.

Scorpio, Angelo ✙ Providence, R. I.; Harvard Medical School, Boston, 1927; affiliated with Rhode Island Hospital in Providence and State Infirmary in Howard; died November 14, aged 55, of acute coronary thrombosis.

Scott, Stuart L., Staunton, Va.; Meharry Medical College, Nashville, Tenn., 1905; died November 11, aged 71, of coronary thrombosis.

Sharkey, William Patrick ✙ Portland, Ore.; University of Oregon Medical School, Portland, 1926; past president of the Portland Society of Obstetrics and Gynecology; served during World Wars I and II; affiliated with St. Vincent's and Providence hospitals; died November 16, aged 51, of heart disease.

Shearer, Henry Jackson, Altheimer, Ark. (licensed in Arkansas in 1907); died in Davis Hospital, Pine Bluff, Nov. 9, aged 81, of cardiac failure with complete heart block.

Sherman, Warren Hunter ✙ Lowell, Mass.; Medical School of Maine, Portland, 1905; an Associate Fellow of the American Medical Association; member of the New England Pediatric Society; on the staff of Lowell General and St. John's hospitals; died Nov. 9, aged 73, of cerebral hemorrhage and generalized arteriosclerosis.

Short, James Edward, Buffalo; University of Buffalo School of Medicine, 1911; member of the American Medical Association; served during World War I; for many years on the staff of the Edward J. Meyer Memorial Hospital; died in Millard Fillmore Hospital November 26, aged 64, of coronary occlusion.

Simmons, Hugh Ludwig ✙ Worcester, Mass.; Tufts College Medical School, Boston, 1916; served during World War I; a captain in the medical reserve corps of the U. S. Army from 1923 to 1933; appointed to the obstetrical service at Worcester City Hospital in 1919, serving for the past 17 years as one of four senior obstetricians; president of the Worcester City Hospital Staff Association; member of the Association of Military Surgeons of the United States; died Nov. 20, aged 58.

Smith, David S., Utica, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died in Lutheran Hospital, Vicksburg, November 30, aged 69, of bronchogenic carcinoma.

Smith, Harry Anthony ✙ Huntington, W. Va.; Medical College of Virginia, Richmond, 1934; formerly practiced in Wheeling, where he was city and county health officer; while in Wheeling he was president and secretary of the Boone County Medical Society and on the staff of the Madison General Hospital; attached to the Veterans Administration Regional Office; died December 8, aged 59, of coronary occlusion.

Sperling, Samuel N., Venice, Calif.; Northwestern University Medical School, Chicago, 1927; died Nov. 10, aged 57, of coronary occlusion.

Stark, Ernest Hanie, Paris, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1900; past president of the Lamar County Medical Society; served in France during World War I; died recently, aged 77, as the result of a cerebral hemorrhage suffered three years ago.

Stevenson, Onnie Earle ✙ Parsons, Kan.; University of Kansas School of Medicine, Kansas City, 1911; formerly county health officer; served as superintendent of State Hospital for Epileptics; died in Menorah Hospital in Kansas City, Mo., Nov. 13, aged 69.

Stillger, Walter Francis ✙ Hicksville, N. Y.; University and Bellevue Hospital Medical College, New York, 1915; served during World War I; surgeon for the fire department of Hicksville; for many years health officer for the town of Oyster Bay; on the staffs of Meadowbrook Hospital in Hempstead and Nassau Hospital in Mineola; died Nov. 10, aged 60, of cerebral hemorrhage, hypertensive cardiovascular heart disease, and chronic glomerulonephritis.

Stookey, Walter M. ✙ Salt Lake City; Marion-Sims College of Medicine, St. Louis, 1898; died November 19, aged 82.

Sudler, Wright S., Baltimore; College of Physicians and Surgeons, Baltimore, 1903; formerly county coroner; died in Towson, Md., November 19, aged 72.

Swinford, Charles Lewis, Cynthiana, Ky.; Hospital College of Medicine, Louisville, 1906; died Nov. 24, aged 66, of cerebral hemorrhage.

Thompson, Louis Levi, Reading, Pa.; Jefferson Medical College of Philadelphia, 1896; died November 28, aged 76, of gangrene of the foot.

Thomson, Robert Strachan ✙ Fitchburg, Mass.; Harvard Medical School, Boston, 1938; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; affiliated with Hospital Cottages for Children in Baldwinsville and Burbank Hospital; died in Evanston, Wyo., November 12, aged 39, in a Union Pacific train accident.

Warren, Melvin George Edward, Seattle; McGill University Faculty of Medicine, Montreal, Canada, 1939; member of the American Medical Association; affiliated with Seattle General and Doctors hospitals; drowned off Orcas Island Nov. 16, aged 42.

CORRECTION

In the obituary of Dr. Dallas Burton Phemister (THE JOURNAL, Jan. 19, page 216) it was incorrectly stated that Dr. Phemister was a vice-president of the International College of Surgeons. He was a vice-president of the International Society of Surgery.

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GOVERNMENT SERVICES

ARMY

Symposium on Trauma.—A symposium on the treatment of trauma in the armed forces will be conducted at the Walter Reed Army Medical Center, Washington, D. C., March 10-12. Sponsored jointly by the Division of Medical Sciences of the National Research Council and the Army Medical Service Graduate School, the symposium is designed to review the problems of trauma in military medicine. Scheduled for discussion are medical organization for handling of trauma in military campaigns and civil disasters, emergency treatment of the wounded, surgical problems related to traumatic injury, rehabilitation of battle casualties, complications related to traumatic injury, and research in military medicine. National and international authorities in these fields will appear on the various programs.

Physicians eligible to attend the symposium include medical officers of the armed forces on active duty, with the exception of those enrolled in the residency training program; full-time civil service physicians on duty at Army installations, physicians and surgeons from other federal agencies, and civilian physicians and surgeons. Army medical officers and civil service physicians at Army installations should make application through the commander of their installation. Applications of other armed forces medical officers should be forwarded through regularly established channels. Applications for all other interested physicians should be forwarded directly to the Commanding General, Walter Reed Army Medical Center, Washington 12, D. C. Applications must reach the commandant of the graduate school by March 1, 1952.

Captain Pocock Awarded the Bronze Star.—Capt. Donald G. Pocock, MC, now assistant professor of military science and tactics at Vanderbilt University, was presented with the Bronze Star medal Jan. 25 for meritorious service in Korea as surgeon of the 96th Field Artillery Battalion. Presentation was made by Col. Robert H. Elliott, professor of military science and tactics at Vanderbilt, in the presence of members of his staff, Tennessee Military District officers, university officials, and friends. Captain Pocock is on the military science and tactics staff for the School of Medicine ROTC Detachment at Vanderbilt.

PUBLIC HEALTH SERVICE

Regular Corps Examination for Medical Officers.—A competitive examination for appointment of medical officers to the regular corps of the Public Health Service will be held on June 3-5 at a number of points throughout the United States. Applications must be received no later than April 30, 1952.

The regular corps is a commissioned officer corps composed of members of various medical and scientific professions, appointed in appropriate categories such as medicine, dentistry, nursing, engineering, and pharmacy. Appointments will be made in the grades of assistant surgeon and senior assistant surgeon. In making assignments, consideration is given to the officer's preference, ability, and experience; however, all commissioned officers are subject to change of station and assignment as necessitated by the needs of the service. Appointments are permanent in nature and provide opportunities to qualified physicians for a life career in clinical medicine, research, and public health. To be eligible for either grade, candidates must be a United States citizen, at least 21 years of age, and a graduate of a recognized school of medicine. The grade of assistant surgeon requires at least seven years of educational training and professional experience subsequent to high school. The grade of senior assistant surgeon requires at least 10 years of educational training and professional experience subsequent to high school.

Applicants who will meet these qualifications within nine months of the date of the written examination will be admitted, but may not be appointed until they fulfill the requirements. Physicians who are successful in the examination and are now serving internships will not be placed on active duty in the regular corps until completion of internship. The examination will include an oral interview, physical examination, and written objective tests covering the professional field. Gross pay is identical to that of officers of equivalent rank in the Army and Navy. Entrance pay for an assistant surgeon with dependents is $5,686.56 per annum; for senior assistant surgeon with dependents, $6,546. These figures include the $1,200 annual additional pay received by medical officers as well as subsistence and rental allowance. Officers on active duty are not eligible to receive disability compensation from the Veterans Administration. Provisions are made for promotion at regular intervals up to and including the grade of senior surgeon (commander) and for promotion by selection to the grade of medical director (captain). Retirement pay after 30 years of service or at the age of 64 is three-fourths of annual basic pay at the time of retirement. Information may be obtained by writing to the Surgeon General, United States Public Health Service, Washington 25, D. C. Attention: Division of Commissioned Officers.

VETERANS ADMINISTRATION

Seminars on Modern Concepts in Psychiatry.—The Veterans Administration Regional Office at 366 West Adams St., Chicago, and the Veterans Administration Hospital at Downey, Ill., five miles south of Waukegan, Ill., have been sponsoring a series of weekly seminars on modern concepts in psychiatry. The seminars will continue until May 28. The speakers and their subjects for the remaining program will be as follows:

On March 18—Dr. Harry C. Solomon, professor of psychiatry, Harvard University Medical School, Boston, will speak on "The Acute Psychoses" at 10 a. m. and 1 p. m. at Downey and at 8 p. m. at the Chicago Regional Office in a joint meeting with the Illinois Psychiatric Society.

On March 26—Dr. Paul H. Hoch, assistant professor of psychiatry, Columbia University College of Physicians and Surgeons, New York, at 10 a. m. and at 1 p. m. at Downey on "The Pseudoneurotic Form of Schizophrenia" and at 8 p. m. at the Chicago Regional Office on "Theoretical and Clinical Aspects of Anxiety."

On April 2—Dr. Harold E. Himwich, director, Research Division, State Research Hospital, Galesburg, Ill., will speak at 10 a. m. and 1 p. m. at Downey on "Functional Organization of the Brain" and at 8 p. m. at the Chicago Regional Office on "Experimental Epilepsy."

On April 8—Dr. L. J. Meduna, professor of psychiatry, University of Illinois College of Medicine, will speak at the Chicago Regional Office at 8 p. m. on "Schizophrenia and Schizophreniform States."

On April 30—Dr. R. B. Suitt, associate in neuropsychiatry, Duke University School of Medicine, Durham, N. C., will speak at 10 a. m. and 1 p. m. at Downey on "Changes in Dart Test Performance Brought About by Prefrontal Leucotomy" and at 8 p. m. at the Chicago Regional Office on "Manifestations of Depression."

On May 7—Dr. Karl M. Bowman, professor of psychiatry, University of California Medical School, will speak at 10 a. m. and 1 p. m. at Downey on "The Problem of Homosexuality" and at the Chicago Regional Office at 8 p. m. on "Children Brought Before the Juvenile Court in Connection with Sex Offenses."

On May 21—Dr. David M. Rioch, technical director, Neuro-Psychiatry Division, Army Medical Service Graduate School, Washington, D. C., will speak at Downey at 10 a. m. and 1 p. m. on "Functions of the Mid-brain" and at the Chicago Regional Office at 8 p. m. on "The Need for an Operational Terminology in Psychiatry."

On May 28—Dr. Henry A. Davidson, of the Veterans Administration, will speak on "Scientific Article Writing" at 10 and 11 a. m. and 1 p. m. at Downey.

Residencies in Psychiatry.—The Veterans Administration Hospital, Lyons, N. J., has available residencies in psychiatry for one to three years that are fully accredited by the American Board of Psychiatry and Neurology. The training can begin at any time in a program of lectures, conferences, and seminars under the direction of the Department of Psychiatry, New York Medical College, and intensive training, both intramurally and through rotation in special hospitals in the adjacent area. There is, in addition, an extensive series by guest lecturers and authorities in neurology, psychiatry and related fields as well as an annual institute at the hospital.

FOREIGN LETTERS

GERMANY

Meeting of the German Society for Research on Circulation.—The 17th meeting of the German Society for Research on Circulation was held from March 30 to April 1. A total of 700 physicians and scientists from most of the European countries participated in the meeting held in the W. G. Kerckhoff Institute in Bad-Nauheim.

Under the chairmanship of Professor Wollheim of Würzburg, the meeting opened with the subject Pulmony Circulation. W. Forssmann of Bad-Kreuznach, who was first to undertake catheterization of the heart, described his self-experimentation of 21 years ago. U. von Euler of Stockholm and von Hayek of Würzburg described the physiology and functional anatomy, respectively, of the pulmonary blood passages. Grosse-Brockhoff of Bonn discussed the hemodynamics of the pulmonary circulation. Grosse-Brockhoff is regarded in Germany as an expert in the evaluation of congenital anomalies of the heart; he advised caution in the use of catheterization. He felt that this method is not without danger and should be used only if diagnosis or treatment demand it and in collaboration with surgical clinics. Bolt and Knipping of Cologne reported their observations on pressure in the pulmonary artery before and after lobar pneumonectomy. They observed temporary increases in pressure after the operation. In emphysema, chronic tuberculosis, and insufficiency of the left side of the heart with stasis, pressures up to 90 mm. of mercury were noted.

On the second day, von Derra of Düsseldorf summarized his results in operations on the heart. The surgical mortality of patients with patent ductus botalli has considerably improved and is now between 0 and 10%. Tetralogy of Fallot accounts for 70% of the cases of permanent cyanosis after the third year of life. The surgical mortality of 15 to 17% is justified, in view of the hopelessness of the defect if left untreated. Valvulotomy in mitral stenosis produces considerable improvement; however, its mortality is still high.

Bein of Basel discussed the pharmacology and Bernsmeier and Esser of Düsseldorf and Stübinger of Bielefeld the clinical results obtained with a ganglion blocking agent, pendiomid* (n, n, n'-n'-3-pentamethyl-N, N'-diethyl-3-aza-pentane-1, 5-diammonium dibromide) in hypertension. It has been helpful also in asthma and migraine.

The third day was devoted to peripheral circulation. Hasse of Halle demonstrated that disease of the pelvic arteries with vascular obstruction can be diagnosed by clinical methods of examination, such as the walking test, the posture test, measurement of skin temperatures, and palpation of the arteries on the abdomen and in the inguinal flexure. He stressed the value of this direct diagnostic method and advised that aortography and arteriography be used only to determine the exact location and extent of vascular closures before surgical intervention, since these are not entirely harmless interventions.

ISRAEL

Revision of Law Governing Licensing of Physicians.—Revision of the present law governing the licensing of physicians is under the joint consideration of the ministries of health and justice. Dating from the days of the British mandate, the present law permits the licensing of anyone who can "satisfy the Director of the Health Department [now the Minister of Health] that he has studied medicine for not less than five years at a recognized University or Medical School and has obtained a diploma." The main revision contemplated is that immigrant physicians who are unable to prove that they have served a year's internship abroad will be required to do so before being licensed. The value of a physician's diploma varies according to the country in which it was issued; in some countries the diploma is awarded after a year's internship and in others, without this training. Graduates of Hebrew University's Hadassah Medical School are required to intern for a year before receiving the diploma.

According to the bill now in preparation, a diploma issued after a year's internship will be deemed sufficient. More drastic changes, such as the setting up of qualifying examinations for candidates for licenses, are not contemplated. The applicant will not be examined on his skill, linguistic ability, or physical fitness; the license granted will be valid indefinitely. One reason for the government's hesitation in making regulations more rigid is the possible deterrent effect on immigration of physicians, especially from the Anglo-Saxon countries. This contingency might, however, be forestalled by granting exemptions to physicians invited to immigrate. Since the establishment of the state, 1,228 licenses have been issued, and in only 24 cases, in which the validity of the diploma was in question, were applications rejected.

Owing to mass immigration, the number of physicians has decreased from 1 for every 260 persons in 1947 to 1 for every 450 persons in 1951. This rate is still twice as high as that for England, which has 1 physician for every 900 persons. However, 45.4% of Israel's physicians are over 50 years old with only 11.2% below 35, as compared with 25% below 35 in the United States. The average age of Israel's physicians is 47. While there is no shortage of physicians in urban areas, the lack is felt in rural settlements. With the exception of the authority to draft physicians into the armed service, the government today has no power to compel physicians to work in specific locations. The Israel Medical Association constantly fought arbitrary restriction of the number of practicing physicians by the Mandatory Health Commissioner, who was empowered to fix an annual quota. The effect of this restriction was to prevent many eminently qualified physicians from following their profession. However, the association today feels that the prevailing official policy is too liberal. It is, accordingly, preparing a proposal that would give the medical association a decisive voice in ruling on each application. A candidate thus refused a license would be able to appeal to the Ministry of Health.

Roentgenography in Amebiasis and Heart Disease.—Prompted by the fact that Israel is in an endemic area for amebiasis, the roentgenography department of Hadassah University Hospital, Jerusalem, began studying, in 1943, the roentgenologic manifestations of amebiasis of the colon, liver, and chest. Some of the observations made have been summarized by Drs. A. Druckmann and S. Schorr, who divided the roentgenographic manifestations of amebiasis of the colon into two types: the diffuse type that is roentgenologically not characteristic and the localized type that is characterized by the length of the colon that is occupied by the filling defect. The lesion is often multiple, and the narrowing of the lumen is incomplete. It was learned that absence of pain during the barium enema is of diagnostic significance. Antiamebic treatment in some cases heals the lesion. In October, 1951, S. Schorr and A. Schwartz published another roentgenologic observation in "Amebiasis of the Liver with Concomitant Findings in the Chest." The roentgenologic manifestations of amebiasis in the liver and thorax, as observed in a series of 49 cases of proved amebiasis, are described. The first changes are limited to enlargement of the liver shadow and restriction of motility and elevation of the right leaf of the diaphragm. Other signs worth noting are localized bulging of the diaphragm on the right side, obliteration of the costophrenic or cardiophrenic angles, pleural effusion, and pneumonic consolidation with or without abscess formation. The authors point out another sign worthy of further investigation: a linear string-like perpendicular shadow in the right lower lung field in ad-

The items in these letters are contributed by regular correspondents in the various foreign countries.

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dition to a fixed and deformed diaphragm. Amebiasis should always be considered in the diagnosis of pathologic conditions in the right side of the chest (pleurisy, empyema, pulmonary abscess, and basal pneumonia), especially in localities in which the disease is endemic.

During the study of the roentgenologic manifestations of the heart, a method of detecting early enlargement of the left atrium was found and was described in a paper entitled "The Recumbent Esophagogram." The authors (S. Schorr and others) reported that with the use of the esophagogram made with the patient recumbent, discrepancies between clinical and roentgenographic detection of early mitral stenosis may be considerably reduced. In view of the satisfactory results obtained, they advocate wider use of this method.

New Hebrew University-Hadassah Medical Center.—A considerable part of the $7,500,000 needed for the erection of the Hebrew University-Hadassah Medical Center in Jerusalem has already been raised, and construction is expected to begin this year. This was reported by Dr. Kalman Mann, newly appointed director general of the Hadassah Medical Organization, at a press conference in Jerusalem. He also announced that, in accordance with the organization's policy of transferring administration of hospitals to local authorities as soon as feasible, a large part of Hadassah's preventive medicine and school hygiene services would be transferred to the Ministry of Health. He reported that 40 preventive medicine stations in Jerusalem and the corridor will be maintained and will serve about 200,000 persons. During the next two or three years basic changes will be introduced into the work of the stations providing prenatal and postnatal care. Some of them will be converted into community health centers, where stress will be placed on health instead of on illness.

The second group of medical students have finished their final examination and are now able to begin their practical work in various hospitals of the country. There were 24 students in this group, all ex-soldiers. Most of them began their medical education abroad and interrupted their studies to join the Israel Defense Forces. After cessation of fighting they were admitted to the medical school. Eighty-seven students have completed their studies at the Hadassah Medical School in Jerusalem since 1950.

Medical Teaching Mission in Israel.—During the months of September and October, 1951, a medical teaching mission operated in Israel on behalf of the World Health Organization and the Unitarian Service Committee. The members of the mission were specialists in the various branches of medical activity. The clinical and preclinical sciences and sanitary engineering were represented. The work of the mission was planned by Dr. Erwin Kohn of Geneva, together with an Israeli preparatory committee. The clinical group visited various hospitals, where they participated in conferences, lectures, and informal discussions with their Israeli colleagues. The preclinical group joined the clinicians in some of the conferences and, in addition, spent considerable time in teaching activities at the Rehovot Institute of Research and the Hebrew University. The public health group studied Israel's various health problems, and held a number of seminars on public health problems.

The mission was a great success, and the work of the public health group proved especially valuable. Israel, at present, is absorbing large numbers of immigrants from various parts of the world having widely varying standards of living. The health problems raised by this mass immigration are enormous, and the advice and guidance of these eminent experts were invaluable contributions toward their solution. The public health group has also contributed toward the long-term health policy of this country by pointing out the dangerous lack of a centralized coordinated plan in the present system in which a number of institutions independently engage in health activities. Dr. Karl Evang, in a farewell address, stated that, in matters of public health, this country is "walking on the edge of a volcano." He issued a plea, on behalf of his colleagues, for coordination and unification of health activities under a centralized authority.

Seventh Israel Pediatric Congress.—The Seventh Israel Pediatric Congress took place in Jerusalem from Dec. 12 to 14, 1951. The main subject of discussion was the condition of the immigrant child. The infant mortality rate for the Jewish population in Palestine in 1947 was 28 in 1,000 births and was among the lowest in the world. The wave of immigrants from primitive countries in Asia and Africa has caused an increase in the mortality and morbidity rates for the new state and has created gigantic problems of an administrative and medical nature for the health authorities. Tuberculosis and skin and eye diseases, widely spread among children of new immigrants, were discussed in lectures. A heavy epidemic of infantile paralysis in 1950, and to a lesser degree in 1951, has aroused great interest and concern about this disease in Israel, which before was almost free of it, except for a few sporadic cases. The epidemiology of this disease and the follow-up of cases in Israel, as well as recent progress in virus research and orthopedic problems, were covered in a second series of lectures. A third group of lectures concerned diagnosis and surgical treatment of congenital heart disease and the experience of local physicians in this field. Another topic of lectures and discussions was prematurity, which also constitutes a major problem of the new state, because of the unusually high number of prematurely born infants and the almost complete lack of special facilities for their care. Related questions of nutrition were discussed, and the need for special stations, personnel, and facilities for transportation were pointed out.

Hysterosalpingography.—For many years, hysterosalpingography has been the subject of special investigation in Hadassah's roentgenography department. Observations made in this field were recently published in a paper entitled "Uterovenous and Uterolymphatic Intravasation in Hysterosalpingography," (A. Druckmann and A. Rozyn). Two distinct phenomena, intravasation and lymphatic transfer, were studied. Lymphatic transfer is characterized by closely reticular turbidity in the uterine wall, slow clearance of oil from the uterine body, accumulation of oil in the regional lymph nodes, and retention of iodized oil (lipiodol®) in the glands for months and even years.

PARIS

Use of Vitamin B_{12} in Neurology.—At the Nov. 16, 1951, meeting of the Medical Society of the Paris Hospitals, Drs. J. Lereboullet and R. Pluvinage reported on the use of vitamin B_{12} in the treatment of 74 patients with neurological disease. In 10 of 43 patients with multiple sclerosis, there were no positive reactions; in 16 patients with advanced cases, there were 4 instances of only subjective improvement. In 17 patients with cases of average intensity, there was noticeable improvement, and, in 4 instances, the patients were able to resume their normal occupations after years of illness and failure of all previous treatment. In eight patients with spastic paraplegia, including two cases of unknown origin and two cases that occurred after serious accidents, functional improvement was observed. In six out of eight patients with spinocerebellar syndromes of the acromegaly type, functional improvement and a diminution of ataxia were noted; four patients, formerly invalids, were able to resume their former activities. In two children with cerebellar atrophy, vitamin B_{12} brought about an ambulatory state and a considerable diminution of objective cerebellar signs. In seven patients with polyneuritis, including three with Korsakoff's psychosis, results were spectacular; the three patients with Korsakoff psychosis were cured within one week. The authors believe that vitamin B_{12} has a positive action on early polyneuritis but has no effect on old lesions. In regard to the mechanism of action of vitamin B_{12}, the authors consider two hypotheses. The first is that vitamin B_{12} acts on myelinic elements, especially in neuroanemic syndromes and in certain cases of multiple sclerosis, in which demyelination, with comparative conservation of axons, occurs. The second hypothesis assumes an occasional direct stimulation of functions of the elements not destroyed.

CORRESPONDENCE

CHARACTER OF STUDENT AMERICAN MEDICAL ASSOCIATION

To the Editor:—"What sort of men are coming up in our ranks?" This question must occasionally come to the physician's mind as the years since his entry into practice slip by. Only a fraction of American physicians can witness the education of the next generation of practitioners. Many doctors work with interns and residents in community hospitals, but a considerable number do not encounter the profession's recruits until there is a new arrival in town or conversations occur at meetings. With the present concern over the moral fiber of youth and reports of disturbing influences on university students, it is reasonable to wonder about the men and women we are training to succeed us in times of social and economic challenge.

Those who are engaged in the tasks of medical education are spared the fears of the general public. Medical students in general have already faced the major postadolescent crises and temptations. They are a carefully selected group who have passed high admission standards that attempt to determine more about an applicant than his academic qualifications. Most medical students have idealistic motivations, whether obvious or latent. These are nurtured in medical school by the principles and the living precept of their elders. Medical schools are dedicated to train men and women to give of their skill for the good in life. As a result of knowing their students well, medical professors come to have faith in them, but recently a new development gives additional justification for that faith. The birth and rapid progress in infancy of the Student American Medical Association is a clear indication of the character of those who follow us. I have had close relations with this new group in its formative first year on local and national levels, and I believe that an impression of its potentialities may be of interest.

The Student American Medical Association has, in one year, come to be the definitive group of the student part of the profession. Despite the need for such a group, previous attempts at a union of medical students failed, because they were either ill-founded or poorly motivated. This time, however, the student founders, representing certain midwestern schools, appealed to the representative body of American medicine for counsel and were supported by instant encouragement from students at leading institutions across the country. Sympathetic support was received from the American Medical Association, and the students found their cause expedited by its instant financial aid and widespread services. This has given the student organization cause for both gratitude and moments of chagrin. Although the new association was propelled into more rapid growth and efficient organization than it might otherwise have enjoyed, this aid gave the strongly individualistic American medical students reason to wonder if the new student group was not to be but a "student front" or a "tool of the senior A. M. A.," as they put it. The relations of the American Medical Association to the student group, as expressed by the former and present executive secretaries, have dispelled these fears. Members may be proud of both the response and the attitude of the A. M. A. The participants from the headquarters staff deserve commendation for making possible effective paternal aid without extreme attachment on the one hand or direction on the other.

Finding that they have a completely student organization, the members set about to make effective contributions while in training. In times of need hitherto unknown, men have suddenly appeared from obscurity to assume leadership of the nation. So have responsible young men and women come from all parts of the country to lead this Association. I recently attended the meeting of the Student House of Delegates. Here I found practical committee members, planners with vision, energetic workers, and even skilled parliamentarians and public speakers. It was gratifying to detect the high degree of knowledge of social, political, and economic trends they possess. It was a pleasant, but not unexpected, surprise to witness the ease with which the dissector or clinical clerk dons the toga and works as a man among men.

The House of Delegates of the Student American Medical Association is a virile, progressive group. Despite their wide geographical origins, the delegates reflect a favorable harmony of thought and the universal nature of student problems. The proceedings of the House of Delegates revealed several important features of the Association's character: a democratic willingness for all to be heard amidst the careful discussion of matters before them; a reluctance to act definitively without thorough investigation; a desire to cooperate with other agencies involved in similar problems of internship selection, selective service, and curricular matters; and cautious reluctance to affiliate with international student professional groups until their aims and programs could be ascertained. Their major theme is one of careful building of long-range programs while working toward certain immediate objectives. Youth is often rebellious and impulsive, but this organization already shows the good judgment and desire to cooperate that one expects with maturity.

It is natural to wonder about the attitude of American medical students toward the future character of medical practice. By acting to support the American Medical Foundation by resolution and by planning a financial contribution from their treasury, the House of Delegates of the Student American Medical Association clearly showed that they are devoted to the medical profession in its historic form of practice as a free and independent enterprise. We occasionally hear of students who feel that governmental control of medicine would be a desirable objective. In the Student American Medical Association there is no indication that any large numbers of our students hold such convictions.

These observations indicate the character of the Student American Medical Association to be one of serious consideration of future obligations as practitioners and citizens. The colleges have trained our students well; the medical schools are developing their skills and molding favorable philosophies. The Student A. M. A. provides them with a long-needed voice and an opportunity to prove that they are well worthy to assume full stature as our colleagues at the appointed time.

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DIAGNOSIS OF MACULAR LEPROSY

To the Editor:—In regard to the article on the diagnosis of leprosy by Dr. Robert K. Maddock, in THE JOURNAL for Jan. 5, 1952 (page 44), I would like to say that for a few years following 1895 my father, Dr. Luis F. Alvarez, was in charge of research in leprosy in Hawaii. After studying at Johns Hopkins, he returned to Honolulu and built up a board of health research laboratory at Kalihi. There he worked for several years trying to find a remedy for leprosy.

He soon devised a method that was highly successful in the diagnosis of the macular form of the disease. With a fine mouse-tooth forceps he would raise a tiny bit of the skin in a suspicious patch and snip it off with sharp scissors. He would drop this into a small mortar with a few drops of water, and, as a boy, it was my job to grind it for a few minutes until it disappeared. The few drops of liquid were then dried on a slide and stained in the usual way with carbolfuchsin. Commonly the acid-fast bacilli were found, and my father came to depend greatly on the test. Unfortunately, he reported it (as I remember) only at the World Lepra Conferenz held in Berlin in 1897, and hence only the leprologists of that time knew of it. Several used it and liked it. I imagine it would be well to use it again, because it was such a simple and successful procedure.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Chiropractors: Rupture of Brain Tumor Following Adjustment.—The plaintiff sued for damages alleged to have been caused by the malpractice of the defendant chiropractor. From a judgment in favor of the plaintiff, the defendant appealed to the Supreme Court of Montana.

The plaintiff was suffering from a stiff neck, headache and sore spot behind the right ear and went to the defendant's office for relief. He took an x-ray of the plaintiff's neck and said that the picture showed that two vertebrae were out of place, and he recommended a series of adjustments to return such vertebrae to their proper position in the spine. The plaintiff testified that on the date of one of these adjustments she got on the table in the defendant's office. "As soon as I was in the right position the thump came immediately, right away, by Dr. Kahle, on the sore spot on the back of the neck. . . . I said 'Oh, that was awful.' I said, 'Something terrible has happened to me.' I said, 'That was awful. Let me up. I don't want any more; I can't stand any more.' He said, 'You will be all right. Let me get this other one.' I said 'I have had enough—don't—stop.' " She testified, further, that after she had told the defendant to stop, he continued to give her further adjustment of her neck and up and down the spine. The plaintiff testified that when she went to the defendant's office for treatment she was able to walk, had good eyesight, carried on normal activities, was strong and able-bodied, and suffered only from a stiff neck, headaches and a sore spot behind the right ear. Immediately after the adjustment, the plaintiff was unable to walk, her vision was impaired, she vomited and was in pain, and suffered a partial paralysis of the throat and vocal chords. She was taken from the defendant's office, on a stretcher, to a local hospital and was subsequently removed to the Mayo Clinic at Rochester, Minn., for examination and treatment. According to the testimony of witnesses from the Mayo Clinic, the plaintiff was suffering from a brain tumor when she visited the defendant's office.

It is one of the fundamental duties of a physician, said the Supreme Court, to make a properly skillful and careful diagnosis of the ailment of a patient, and if he fails to bring to that diagnosis the proper degree of skill or care, and makes an incorrect diagnosis, he may be held liable to the patient for the damage thus caused just as readily as he must answer for the application of improper treatment. No good reason exists why the law applicable to physicians, surgeons, dentists, and the like, should not also apply to chiropractors.

Physicians and surgeons who were called by the plaintiff and who were competent to read x-ray pictures of the spine, testified, after examining the x-ray picture of the plaintiff's neck taken by the defendant, that such picture showed no vertebrae out of place. They also testified that other x-ray pictures of the plaintiff's neck taken after she reached the hospital on the day of the adjustment, showed no vertebrae to be out of place. From the evidence in this case, said the Supreme Court, the jury could find the defendant made a wrong diagnosis or analysis of plaintiff's condition, and that her stiff neck, headaches and sore spot behind the right ear were not due to vertebrae out of place; that there were no vertebrae out of place and the x-ray picture, taken by the defendant, so showed; and that defendant should have given plaintiff no adjustment. Continuing, the court said that the jury could also find that during the adjustment, after the plaintiff directed the defendant to stop, the defendant continued adjustment and manipulation with his hands and caused a rupture of a brain tumor, resulting in injury to the plaintiff.

In view of the fact that the jury was warranted in making the above findings, the Supreme Court was of the opinion that the verdict of the jury was not against the weight of the evidence. Accordingly the judgment in favor of the plaintiff was affirmed. *Bakewell v. Kahle, 232 P. (2d) 127 (Montana 1951).*

Admissibility in Evidence of Chemical Tests for Intoxication.—The defendant was convicted of the offense of driving a motor vehicle upon a public highway while intoxicated and appealed to the court of criminal appeals of Texas.

After the defendant's arrest, he was taken to a hospital where a blood specimen was taken from him. At the trial which followed, a chemist for the Department of Public Safety testified that the defendant's blood contained 3.6 mg. of alcohol per cubic centimeter and a physician testified that 1.5 mg. of alcohol per cubic centimeter or more, in the blood would render a person intoxicated. This testimony was admitted in evidence over the defendant's objection that the specimen was taken from him without his voluntary consent and by coercion and persuasion, that the specimen was taken without the warning required under the confession statute having been given and while the defendant was in custody, and that the admission of evidence of the results of the blood test was tantamount to compelling the defendant to give evidence against himself.

The evidence shows, said the court of criminal appeals, that the blood which was taken from the defendant was taken with his consent at the hospital and by a nurse. When a specimen is taken by competent and trained nurses, doctors or laboratory technicians with the consent of one whose sobriety is questioned, the court continued, the results of a blood test thereof may be introduced by the state or by the accused. Consent to the taking of the specimen being shown, the provisions of the fifth amendment to the Constitution of the United States and Art. 1, Sec. 10 of the Constitution of Texas, Vernon's Ann. St. Const., providing that no person shall be compelled to give evidence against himself, are not violated. The purpose of the confession statute referred to by the defendant, said the court, is to prevent the use of verbal statements in the nature of a confession made by an accused while under arrest, and which do not come within the exceptions named in the statute. The provisions requiring that the accused be warned before the confession is made have no application to the obtaining of his consent for blood to be taken for the purpose of analysis.

The defendant's conviction was reversed, however, because there was no showing that the specimen taken by the nurse at the hospital was the same specimen as was examined by the chemist for the Department of Public Safety. *Brown v. State, 240 S. W. (2d) 310 (Texas 1951).*

MEDICAL MOTION PICTURES

Good Eating Habits: 16 mm., black and white or color, sound, showing time 10 minutes. Produced in 1951 by Coronet Instructional Films with the assistance of Clifford J. Barborka, M.D., and James R. Wilson, M.D. Procurable on purchase from Coronet Instructional Films, Coronet Building, Chicago 1.

This is an attitude building film meant to provide reasons for developing good eating habits, which can be understood by children. The story of the film concerns the eating habits of a boy on two succeeding days. On the first day he hurries through breakfast and lunch. He has been given money to buy soup for his lunch, but he spends this for pop and candy after school. Then he is unable to eat the well-prepared dinner his mother has waiting for him, and the results are a stomach-ache and an early bedtime. The next day he eats breakfast leisurely, takes ample time to eat his sandwiches, and uses his lunch money for soup rather than pop and candy. At dinner he is ready and able to eat a good meal. The results of these better habits are that he is not hungry between meals and he feels more like studying and playing hard.

It is not within the purpose of this film to discuss or show food selection and preparation. The facts presented are reasonably accurate but somewhat unrealistic, in that a single attack of indigestion apparently entirely changes the eating habits. The photography and narration are well done. By itself, the film is not completely convincing; however, when used with supplementary teaching materials and elaboration, it is recommended to stimulate discussions in the elementary and junior high grades and also in parent groups.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Neurology and Psychiatry, Chicago

66:669-816 (Dec.) 1951

Subcortical Connections of Temporal Pole in Relation to Temporal Lobe Seizures. C. A. Marsan and J. Stoll Jr.—p. 669.
Acute Vascular Lesions of Brain Stem: Complication of Supratentorial Space-Occupying Lesions. B. W. Cannon.—p. 687.
Observations on Effect of Corticotropin in Schizophrenia: Preliminary Report. G. H. Glaser and P. H. Hoch.—p. 697.
Amnesia—Its Integrative Analysis in Psychopathological Orientation. L. J. Siegel.—p. 700.
Studies on Excretion of Total Neutral 17-Ketosteroids in Schizophrenic Patients. S. P. Gottfried and I. Minsky.—p. 708.
*Tetany and Epilepsy. H. Gotta.—p. 714.
*Papilledema in Poliomyelitis. C. G. Weiman, F. H. McDowell and F. Plum.—p. 722.
Boeck's Sarcoid with Involvement of Central Nervous System. W. H. Pennell.—p. 728.
Forced Crying and Laughing: Treatment with Atropine and Atropine-Like Agents. R. Cohn.—p. 738.
Papilledema in Guillain-Barré Syndrome. A. L. Frew and K. R. Magee. —p. 744.
Hemiplegia and Thrombosis of Internal Carotid System. A. R. Elvidge and A. Werner.—p. 752.
Electric Shock Therapy in Case of Myasthenia Gravis Complicated by Schizophrenic Psychosis. R. L. Williams and M. Silbermann.—p. 783.

Tetany and Epilepsy.—Some clinicians regard tetany and epilepsy as completely separate entities that may occur in the same patient, but others assume that tetany is the cause of epilepsy when both conditions are present. The author previously had made electroencephalographic studies on 14 patients with tetany. In this paper he describes six cases of tetany (four postoperative and two idiopathic) in which typical symptoms of epilepsy occurred. He concludes that tetany and epilepsy are separate entities. When they occur together, epilepsy follows tetany. In subjects with an epileptic constitution hypocalcemia precipitates epileptic seizures. Abnormalities in the electroencephalograms of these patients appear in all the leads (frontal, parietal, and occipital); they extend throughout the cortex and are no different from disturbances observed with other types of epilepsy. In all cases of epilepsy of unknown origin, the possibility of parathyroid insufficiency should be considered; symptoms of tetany should be looked for, and the concentration of blood calcium and inorganic phosphate should be determined. In these cases treatment with barbiturates gives no results, but the blood calcium level should be increased by means of calciferol or dihydrotachysterol (Holtz's "A. T. 10"), which gives excellent results if administered long enough in adequate doses.

Papilledema in Poliomyelitis.—Five patients recovering from poliomyelitis accompanied by moderate to severe quadriplegia were found to have papilledema during early convalescence. Papilledema was first observed 11 to 48 days after the acute onset of the illness and persisted from 13 to 140 days, with an average duration of 60 days. It was a benign and self-limited complication. Each patient complained of double vision, and one had associated headache. The visual acuity and visual fields were normal in all five patients. The spinal fluid pressure was elevated in the three patients in whom it was measured. Papilledema in these patients probably represented part of a generalized edema in the central nervous system associated with infection.

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Titles marked with an asterisk (*) are abstracted.

A.M.A. Arch. Surgery, Chicago

63:585-714 (Nov.) 1951

Experimental Surgical Techniques in Mitral Stenosis. E. Marcus.—p. 586.
Some Studies on Clotting Activity of Extracts of Normal and Diseased Tissues. A. Blaustein, C. Huber and M. Alberian.—p. 592.
Increased Intracranial Pressure Following Radical Neck Surgery. R. K. Jones.—p. 599.
Experimental Artificial Left Heart for Exposure of Mitral Stenosis. A. Kantrowitz, E. Hurwitt and A. Kantrowitz.—p. 604.
Postcholecystectomy Complications Due to Incomplete Removal of Gallbladder and Cystic Duct: Report of Case of So-Called Reformed Gallbladder. W. B. A. J. Bauer.—p. 612.
*Endometriosis of Vermiform Appendix: Review of Literature with Addition of Nine New Instances, One of Which Caused Severe Melena. D. C. Collins.—p. 617.
*Ligation of Hepatic and Splenic Arteries in Patient with Atrophic Cirrhosis of Liver. J. K. Berman, L. P. Muller, C. Fisch and W. Martz. —p. 623.
Diverticulum of Left Ventricle of Heart: Review of Literature and Report of Successful Removal of Diverticulum. S. Skapinker.—p. 629.
Internal Biliary Fistula Due to Peptic Ulcer. J. M. Sullivan and L. Hamman.—p. 635.
Effect of Intraperitoneally Injected Benzalkonium (Zephiran®) Chloride. W. P. Kleitsch and C. F. Heider Jr.—p. 641.
Cortisone or Corticotropin for Asthmatic Patients Who Require Major Surgical Procedures. L. E. Prickman, G. A. Koelsche, H. M. Carryer and others.—p. 647.
Tuberculosis Originating from Contaminated Suture Materials and Plastics: Experimental Study. H. J. Corper and M. L. Cohn.—p. 652.
Thyroiditis. C. P. Schlicke.—p. 656.
Challenge of the Foreign Body. E. P. Lehman.—p. 663.
Complications of Intramedullary Fixation of Fractures of Femur. W. G. Stuck and M. S. Thompson.—p. 675.
*Vagotomy in Treatment of Biliary Dyskinesia. G. Crile Jr. and D. W. Miller.—p. 687.
Failure of Thymectomy in Lymphatic Leukemia. G. O. Dean, A. M. Earle and W. A. Reilly.—p. 695.

Endometriosis of Vermiform Appendix.—Collins summarizes the data reported in the literature on 134 cases of endometriosis of the vermiform appendix. One case is presented in greater detail because of its unusual clinical features. This apparently is the first recorded instance of severe melena resulting from appendical endometriosis. Marked secondary anemia developed within three months following the onset of symptoms. The patient remained well after an appendectomy.

Ligation of Hepatic and Splenic Arteries in Cirrhosis.—Experimental work having shown that ligation of the hepatic and splenic arteries was a rational procedure in the treatment of portal hypertension due to cirrhosis of the liver, it was decided to try the operation on a patient with advanced cirrhosis. He was a man of 60, who for about 30 years had consumed 6 to 10 bottles of beer and 1 to 2 pt. (0.5 liter) of whisky daily. During his first hospitalization in 1949 numerous paracenteses were done, with removal of an average of 17,855 cc. of fluid per month. Then he was treated for five months with a carboxylic type of cation exchange resin in doses ranging from 40 to 90 gm. per day. With this therapy his weight remained relatively constant, only one paracentesis being necessary during this time. Because of anorexia, weakness, and bloody diarrhea, the patient returned to the hospital on April 30, 1950, and the resin therapy was discontinued. Persistent bloody diarrhea associated with a small liver indicated a grave prognosis. During the next six months therapy consisted of a low salt diet and daily injections of mercurial diuretics, but monthly paracenteses were still necessary. On Nov. 21, 1950, the abdomen was opened and approximately 7,500 cc. of straw-colored fluid was aspirated from the abdominal cavity. The liver was small and hard and was covered with a fibrinous exudate. The hepatic artery was doubly ligated and the splenic artery was also ligated, both vessels being tied close to the celiac axis. Up to the time of this report (six months after the ligation), there has been no edema and only slight recurrence of ascites, which receded as soon as a restricted salt diet was instituted. There are indications of increased urinary excretion of sodium. No bleeding has occurred from the esophageal varices or other points in the gastrointestinal tract. The

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patient has shown remarkable improvement. Perhaps even better results may be obtained by dividing the arteries instead of simply ligating them, so that recanalization cannot occur. This has been done successfully in five patients recently.

Vagotomy in Biliary Dyskinesia.—Postcholecystectomy colic, or biliary dyskinesia, is a poorly defined syndrome. Some clinicians assume that spasm of the sphincter of Oddi is involved. It may cause symptoms indistinguishable from biliary colic due to a calculus, and the possibility of stone in the stump of the cystic duct, stone in the common duct, and disease of adjoining viscera (duodenal ulcer, recurrent pancreatitis, and renal calculi) must be excluded. Most of the treatments employed are aimed at relaxing spasm of the sphincter of Oddi. Antispasmodics including glyceryl trinitrate may be used, but β-diethylaminoethyl fluorene-9-carboxylate (pavatrine®) hydrochloride or adiphenine (trasentine®) hydrochloride seem most effective. Morphine causes the sphincter to contract and should be avoided. Endocholedochal sphincterotomy, splanchnic nerve section, denervation of choledochus, and removal of a long stump of the cystic duct have been tried as surgical treatment. Since the parasympathetic nervous system through the right vagus nerve has tonic control of the sphincter of Oddi, vagotomy on the right side should relax the spasm. Crile and Miller performed nine vagotomies for biliary dyskinesia. Cholangiograms were made on all but one patient, and the diagnosis of biliary dyskinesia was made by exclusion of organic disease. Five of the nine were subjected to bilateral vagotomy, with good results in three, improvement in one, and failure in one. The remaining four were treated by vagotomy on the right alone, with relief of symptoms in one and slight improvement or failure in three. Patients in whom biliary dyskinesia develops usually are nervous and subject to conversion neuroses. Whenever possible, the symptoms should be controlled by medical or psychiatric therapy.

American Journal of Clinical Pathology, Baltimore

21:999-1100 (Nov.) 1951

*Blastomycosis. J. Schwarz and G. L. Baum.—p. 999.
Studies on Platelets: I. Relationship of Platelet Agglutination to Mechanism of Blood Coagulation. M. Stefanini and J. H. Silverberg.—p. 1030.
Estimation of Lysozyme in Certain Biologic Materials. B. H. Pringle, D. C. DePaulis and T. D. Pemrick.—p. 1039.
Clinical Evaluation of Middlebrook-Dubos Hemagglutination Test. R. M. Young and W. A. Leonard Jr.—p. 1045.
Electrocardiographic Changes in Donors During Bloodletting. I. Hoffman, J. Litwins and L. Sussman.—p. 1051.

Blastomycosis.—According to Schwarz and Baum blastomycosis is produced by Blastomyces dermatitidis, a biphasic fungus. They present data obtained in 22 cases observed in Cincinnati during the past eight years, and in 36 cases from the files of the Armed Forces Institute of Pathology in Washington. The only absolute diagnostic proof of the disease is obtained by culture. However, demonstration of double-walled, single-budding yeast cells 5 to 20 μ in diameter in exudates or tissues is acceptable proof. Identification of a culture of Blastomyces largely depends on the structure and the biphasic character of the growth. The organism should not be confused with Torula (Cryptococcus neoformans), as has been done in some reports. The capsule formed by Cryptococcus, which is absent in Blastomyces, is one of the differentiating characteristics. Confusion with Monilia and endospores of Coccidioides immitis is also possible. Skin tests for blastomycosis, the pathological anatomy of the pulmonary and other forms, the pathogenesis, clinical data, and treatment are discussed. Blastomycosis, a chronic granulomatous disease, is most frequently pulmonary in origin. A tendency to heal is common in the lung and satellite lymph nodes and to some degree in other organs. The disease extends by lymphatic, hematic, or canalicular routes, the hematogenous route being most important. Any organ may be involved. Blastomycetes were repeatedly seen in blood vessels, and once in a blood vessel of an organ (kidney) without blastomycotic granuloma. Blastomycetes were also found in bone marrow. Blastomycotic bronchitis (destruction of bronchial mucosa) in smaller bronchi is a constant finding in cases of active pulmonary disease, and perforation into the parenchyma of the lung has been observed. Cutaneous blastomycosis is most frequently secondary to a primary pulmonary infection. The role of trauma has been overemphasized in cutaneous blastomycosis. In pulmonary blastomycosis cavities are uncommon and when present are small necrotic foci without prominent walling-off; pleuritis is always present and is usually dry and fibrinous. Blastomycosis seems to be transmitted by way of the respiratory tract, but the source of infection is unknown. Skin-testing of contacts did not produce evidence for transmission of the disease from man to man. Treatment with iodides is empirical, and antibiotics apparently are of no help. There is little proof that desensitization with vaccine is beneficial. Surgery was of value in four patients with isolated cutaneous lesions.

American J. Digestive Diseases, Fort Wayne, Ind.

18:323-348 (Nov.) 1951

Influence of Virus Hepatitis on Morphology of Gastric Mucosa. E. D. Palmer.—p. 323.
Heredity and Diabetes. E. M. Watson and M. W. Thompson.—p. 326.
Evaluation of Clinical Methods in Gastro-Intestinal Disease: IV. Autopsy Findings of Liver Disease (Fatty Infiltration, Hepatic Cirrhosis) Observed in Peptic Ulcer Cases. A. A. Goldbloom, A. Lieberson and A. Silver.—p. 330.
Gastric Ulcer: Diagnostic Studies in 100 Cases. J. A. Hagans and M. C. McCord.—p. 335.
Gallbladder Disease in Men: Need for Earlier Diagnosis and Treatment. S. Hyman and F. Steigmann.—p. 337.
Use of Multiple Intestinal Adsorbents as Adjunct in Management of Nausea and Vomiting in Pregnancy. V. deP. Fitzpatrick, R. E. Hunter and C. E. Brambel.—p. 340.

American Journal of Ophthalmology, Chicago

34:1483-1648 (Nov.) 1951

Integrated and Buried Implants. A. P. Drucker, W. W. Kreft, M. D. Pearlman and others.—p. 1483.
*Effect of Sunglasses in Protecting Retinal Sensitivity. R. H. Peckham and R. D. Harley.—p. 1499.
Tarsitis as Cause of Sulfonamide Resistance in Trachoma. F. N. Sezer.—p. 1508.
Tumor of Lacrimal Glands: Report of Four Cases. A. R. Irvine, W. L. Roberts and P. S. Soudakoff.—p. 1511.
Mixed Tumor of Lacrimal Gland with Extensive Metastases. W. W. McKinney and W. C. Butz.—p. 1519.
Changes in Corneal Curvature Following Cataract Extraction. G. Floyd.—p. 1525.
Lint in Anterior Chamber Following Intraocular Surgery. D. Vail.—p. 1533.
Glaucoma Associated with Polycystic Kidney Disease. W. L. Berkley.—p. 1539.
Relation of Perceived Size of Half-Images at Fusion Level to Projection on the Horopter: Its Importance in Aniseikonia and Heterophoria. P. W. Miles.—p. 1543.
Ocular Pemphigus: Report of a Classical Case. P. M. Corboy.—p. 1561.
Correlation of Surgical Treatment of Essential Hypertension with Blood-Pressure Response Tests and Retinal Changes. S. D. Aiken.—p. 1565.
Ocular Manifestations of Tropical Diseases. J. M. Varas Samaniego.—p. 1574.
Etiology of Angular Conjunctivitis. Y. Mitsui, S. Hinokuma and C. Tanaka.—p. 1579.
Malignant Exophthalmos. M. M. Medine.—p. 1587.
Clinical Trial of Aureomycin in Trachoma. R. Naccache.—p. 1591.
Preliminary Report on New Cycloplegic and Mydriatic Drug. R. D. Kiess and F. B. Fralick.—p. 1593.

Sunglasses to Protect Retinal Sensitivity.—The need for visual efficiency during night lookout and sentry duty directed attention to retinal sensitivity. It was learned that exposure to excessive sunlight would seriously decrease night vision, and experiments were undertaken on life guards. They were divided into two groups, depending on whether they stated that they wore sunglasses "always" or "usually," or wore them "seldom" or "never." The following conclusions are drawn from the experimental data: 1. Wearing sunglasses of commercial density (35 to 50%) will protect retinal sensitivity for short periods (one day or less), but not for periods of a week or more. 2. Wearing darker sunglasses will provide protection from exposure to excessive sunlight for as long as a week or more. (Such sunglasses are commercially available, but are in the minority). 3. Failure to wear sunglasses will reduce retinal sensitivity by average of about 50%; in extreme cases the loss can amount to more than 90%. 4. Loss of retinal sensitivity can be assessed as a reduction of the effectiveness of available ambient photopic (cone) illumination. 5. Extravisual rays (ultraviolet and infrared) cannot be considered the cause of loss of retinal sensitivity; rather the visible portion of solar radiation is responsible. The

loss of retinal sensitivity after exposure without sunglasses can be a causative factor of industrial and automobile accidents. Night driving after a day at the beach can be dangerous. A small reduction of the effective brightness of fluoroscopic images is a detriment to a radiologist. When fluoroscopy is practiced extensively, use of high density sunglasses is essential. The authors call attention to the difficulty of obtaining sufficiently dark sunglasses. If the wearer's eyes can be seen behind the lenses, the lenses are probably not dark enough.

American Journal of Public Health, New York

41:1333-1454 (Nov.) [Part I] 1951. **Partial Index**

Public Health and "Socialized Medicine." W. P. Shepard.—p. 1333.
Studies of Coxsackie Viruses: Observations on Epidemiological Aspects of Group A Viruses. R. M. Cole, J. A. Bell, E. A. Beeman and R. J. Huebner.—p. 1342.
Brill's Disease: IV. Study of 26 Cases in Yugoslavia. E. S. Murray, T. Pšorn, P. Djaković and others.—p. 1359.
Public Health Aspects of Water Fluoridation. H. E. Hilleboe and D. B. Ast.—p. 1370.
Culture Medium for Detecting and Confirming Escherichia Coli in 10 Hours. G. H. Chapman.—p. 1381.
Public Health Administration in Mental Hygiene. P. V. Lemkau.—p. 1382.
Biostatistics in Evaluation of Premature Services. F. J. Menchaca. —p. 1388.

41:1-126 (Nov. [Part II]) 1951. **Partial Index**

Practical Aspects of Coördinating Maternity Care: Role of Health Departments. J. Whitridge Jr.—p. 5.
Maternity Service Under Health Insurance Plan of Greater New York. G. Baehr and N. R. Deardorff.—p. 44.
Objectives and Methods of the New York City Hospital Consultation Program. S. M. Wishik.—p. 68.
Role of Hospital Consultation Program in Prevention of Prematurity and the Deaths of Prematures. J. B. Faison.—p. 76.
Obstetric Aspects of the Hospital Consultation Program. E. M. Gold. —p. 80.
Role of the Pediatrician in the Hospital Consultation Program. H. M. Wallace.—p. 87.
What and How Shall We Teach Expectant Parents? Point of View of the Pediatrician. M. E. Mercer.—p. 107.

American Journal of Surgery, New York

82:533-670 (Nov.) 1951

Lipomatous Hypertrophy of Ileocecal Valve. M. Edwards and H. Zangara. —p. 533.
Rare Anomaly of Rectum and Lower Urinary Tract. F. J. Burns, L. J. Stephens and H. H. Kramolowsky.—p. 538.
New Horizons in Proctology: The Third Joseph McDowell Mathews Memorial Oration. F. C. Yeomans.—p. 542.
Adenoma of Rectum and Lower Portion of Sigmoid: Clinicopathologic Study. W. L. Cooper, L. A. Buie and J. R. McDonald.—p. 546.
Maximal Diagnostic Potential of Barium Enema in Management of Colon Disease. J. A. Ferguson.—p. 553.
Amino Acid Therapy for Pruritus Ani. L. G. Bodkin.—p. 557.
Surgical Management of Idiopathic Pruritus Ani. G. L. Kratzer.—p. 560.
*Streptomycin in Treatment of Anorectal Tuberculosis: With Particular Reference to Topical Therapy. I. Skir, N. L. Freund and J. M. Gross. —p. 564.
Prophylactic Oophorectomy with Resection of Large Bowel for Cancer. C. A. V. Burt.—p. 571.
Total Hysterectomy with Resection of Primary Carcinoma of Bowel: Report of 47 Cases. R. B. Cattell and A. J. Mace.—p. 578.
Diverticulosis and Diverticulitis: General Consideration and Sigmoidoscopic Diagnosis. N. D. Smith.—p. 583.
Roentgenologic Aspects of Diverticulitis and Its Complications. R. Wigh and P. C. Swenson.—p. 587.
Intestinovesical Fistula. G. H. Ewell.—p. 597.
Surgical Aspects of Diverticulitis. N. W. Swinton.—p. 603.
Benign Lymphoma of Rectum. B. F. Sniderman.—p. 611.
Proctalgia Fugax. J. D. Karras and G. Angelo.—p. 616.
Role of Arteries and of Posture in Hemorrhoids. V. C. Tucker.—p. 626.
Melanosis Coli: Experimental Observations on Its Production and Elimination in 23 Cases. G. S. Speare.—p. 631.
Consideration of Newer Antibiotics. W. E. Herrell.—p. 638.
Rectal Complications Following Treatment of Genitourinary Cancer. O. T. Evans.—p. 645.

Topical Use of Streptomycin in Anorectal Tuberculosis.—When Skir and associates began topical application of streptomycin in anorectal tuberculosis in December, 1946, they found few references to the topical use of streptomycin and none to this method in anorectal tuberculosis. Because of its relative stability in solution, rapid action even in the presence of blood, serum, or pus, and relatively low degree of irritation, they decided to try topical application. The histories of 21 patients treated between December, 1946, and November, 1949, are briefly presented. Streptomycin was first employed as an ointment (33,000 units per gram). In October, 1947, this was abandoned in favor of an emulsion in cod liver oil (2,000 units per cubic centimeter) applied on gauze packing. In November, 1948, the authors changed to a saline solution in the same concentration, which was used for irrigation or to saturate gauze packing. The antibiotic was frequently administered intramuscularly during the latter part of this study as it became more readily available, but always only on the basis of the status of the pulmonary lesion. The authors feel that a statistical evaluation of their results would be meaningless in view of differences in the virulence and sensitivity of various strains, bacterial contaminants, dilution by discharges, and variation in the application. They found, however, that with streptomycin therapy wounds dormant for weeks promptly resumed activity. Burrowing was arrested but fibrosis and vascularization were stimulated, and epithelization and healing generally were accelerated. The intramuscular route seems the most dependable because it allows regular administration and certainty of absorption and systemic effect. The drug is most effective in an aqueous medium. To avoid sensitization, which occurred in three cases, it seems advisable to discontinue local applications after two or three weeks. While topical streptomycin treatment is a valuable adjuvant, surgery remains the basic treatment.

American Review of Tuberculosis, New York

64:477-582 (Nov.) 1951

*Plastic Reconstruction of Trachea and Bronchi. D. L. Paulson.—p. 477.
Histologic Study of Blood Vessels in Surgically Resected Tuberculous Lungs. J. Denst, A. Hurst and S. H. Dressler.—p. 480.
Value of Follow-Up Studies of Children with Primary Tuberculosis. E. M. Lincoln.—p. 499.
Effect of Adrenocorticotropic Hormone (ACTH) on Pneumonia Induced with Tuberculin in Lungs of Sensitized Rabbits. O. M. Reinmuth and D. T. Smith.—p. 508.
Attempts at Passive Transfer of Tuberculin Type of Sensitivity with Living Granulocytes. W. F. Kirchheimer, A. R. Hess and R. G. Spears. —p. 516.
Relationship Between Virulence of Tubercle Bacilli and Vigor of Their Oxidative Attack upon Certain Substrates. L. H. Geronimus and J. M. Birkeland.—p. 520.
Relation Between Size of Infecting Dose of Tubercle Bacilli and Survival Time of Mice. G. P. Youmans and A. S. Youmans.—p. 534.
Assessment of Antituberculous Chemotherapeutic Activity in Mice, Using Virulent Human-Type Tubercle Bacilli. G. P. Youmans and A. S. Youmans.—p. 541.
Blood Media for Culturing Tubercle Bacilli: Evaluation by Means of Serial Dilution Method. A. W. Frisch and M. S. Tarshis.—p. 551.
Subcutaneous Administration of Sodium Salt of Para-Aminosalicylic Acid in Treatment of Tuberculosis. B. M. Fisher, G. Roberts and H. C. Hinshaw.—p. 557.

Plastic Reconstruction of Trachea and Bronchi.—Reconstruction of the bronchial or tracheal lumen may be necessary to preserve lung tissue or life itself, since trauma, tumors, tuberculosis, and other infections may obstruct the lumen. Paulson reviews experimental and clinical experiences with reconstruction of the trachea and bronchi and reports three cases in which he used dermal grafts. The first patient sustained a severe chest injury when heavy drill pipe rolled across his chest and neck. Tension pneumothorax and mediastinal emphysema developed, necessitating an emergency mediastinotomy and pleural decompression. The lung expanded well, but seven weeks later progressive atelectasis became evident. Bronchoscopy and bronchography at this time revealed complete occlusion of the right main bronchus at the carina. To save the right lung, a plastic reconstruction of the right main bronchus was accomplished by a dermal graft. Narrowing of the bronchus by scar tissue did not interfere with normal pulmonary function. In the second case, in which the patient had tracheal carcinoma, tracheotomy should have been done at the time of the reconstruction, as frequent intratracheal aspirations did not adequately remove the secretions. In the two days before tracheotomy was done, the lung was irreversibly damaged by obstruction of smaller bronchi. The third patient developed a tracheal stenosis, secondary to a tracheobronchial tuberculosis. Plastic reconstruction of the upper portion of the trachea by dermal graft was successful, but reactivation of submucosal tuberculosis produced bronchial obstruction, resulting in death. Bronchoscopy three weeks following reconstruction of the trachea revealed a satisfactory

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mucosal lining. The patient had obtained complete relief from tracheal stridor and exercise tolerance had returned to normal. The author believes wire-enforced dermal grafts are satisfactory for plastic reconstruction of the trachea and bronchi.

Annals of Allergy, Minneapolis

9:703-836 (Nov.-Dec.) 1951

Pulmonary Distribution of Radioactive Particles in Rabbits After Inhalation and Intravenous Injection. G. V. Taplin, J. S. Grevior, M. L. Gautschi and others.—p. 703.
Allergy of Urinary Tract: Critical Review of Literature with Analysis of 613 Cases of Uroiogic Disease in Relation to Allergy. S. C. Dees and E. C. Simmons.—p. 714.
Phenergan: Clinical Evaluation: Based on Study of 193 Allergic Patients. M. M. Peshkin, H. G. Rapaport and S. Grosberg.—p. 727.
Studies on Urinary Excretion of 11-Oxycorticosteroids by Allergic Patients Treated with Adrenocorticotropic Hormone (ACTH). A. J. Stanley, G. S. Bozalis, D. H. Huff and others.—p. 741.
Endocrine Hypersensitivity. L. Meltzer.—p. 753.
Differential Diagnosis of Cough in Tuberculosis and Bronchial Asthma. E. A. Brown.—p. 760.
New Sympathomimetic Amine ("Neosuprel") in Treatment of Bronchial Asthma. J. A. Herschfus, E. Bresnick, L. Levinson and M. S. Segal. —p. 769.
Periorbital Dermatitis. B. Swinny.—p. 774.

Annals of Surgery, Philadelphia

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Development of Surgery for Cancer of Colon. A. W. Allen.—p. 785.
Benign Extrahepatic Biliary Tract Obstruction: Analysis of 54 Cases. R. D. O'Malley, A. H. Aufses Jr. and A. O. Whipple.—p. 797.
Experimental Reconstruction of Extrahepatic Biliary System Using Free Venous Grafts. A. E. Pearce, A. W. Ulin, J. H. Entine and G. F. Froio.—p. 808.
*Results of Splenectomy: Follow-Up Study of 140 Consecutive Cases. E. M. Miller and A. B. Hagedorn.—p. 815.
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Technic and Results of Dependent, Greater Curvature Gastro-Enterostomy. R. S. McCleery, J. E. Kesterson and J. N. Proffitt.—p. 844.
Acute Pancreatitis, Diagnosis and Treatment. W. E. Sullens and M. E. Lichtenstein.—p. 853.
Local Recurrence Following Surgery for Cancer of Breast. E. W. Demaree—p. 863.
Experimental Studies of Preserved Aortic Homografts. C. C. Coleman Jr., R. A. Deterling Jr. and M. S. Parshley.—p. 868.
Therapeutic Effect of Aureomycin in Experimental Peritonitis in Dog: II. Parenteral Therapy. F. B. Schweinburg, P. Glotzer, A. M. Rutenburg and J. Fine.—p. 878.
Metabolic Effects of Paracolon Bacteremia. R. M. Nelson.—p. 885.
Use of Skin Grafts in Hernia Repair. W. M. Eisele and G. B. Starkloff. —p. 897.
Total Pancreatectomy for Sarcoma of Pancreas. H. E. Feather and C. L. Kuhn.—p. 904.
Embolectomy in Acute Mesenteric Occlusion. A. A. Klass.—p. 913.
Experimental Evaluation in Dog of Esophagogastrectomy for High-Lying Gastric Ulcer: Preliminary Report. L. B. Kiriluk and K. A. Merendino. —p. 918.
Sacculated Aneurysm of Saphenous Vein. K. M. Lippert and L. D. Frederick Jr.—p. 924.

Results of Splenectomy.—Miller and Hagedorn investigated the records and ascertained the present status of 140 consecutive patients who had undergone splenectomy at the Mayo Clinic from 1942 to 1944. Cases in which the spleen was removed as a secondary procedure or for traumatic splenic rupture were not included. Preoperatively 38 of the 140 cases were diagnosed as congenital hemolytic icterus; 47 as essential thrombocytopenic purpura; 45 as Banti's disease or congestive splenomegaly; 5 as acquired hemolytic anemia; and 5 as "indeterminate splenomegaly." The authors feel splenectomy can be performed for any of the conditions associated with hypersplenism with a reasonably low mortality rate. An exception to this statement is congestive splenomegaly, in which the operation has a higher mortality rate than with the blood dyscrasias. In this series of 140 splenectomies there were six deaths, a mortality rate of 4.3%. Success of splenectomy for hypersplenic disorders frequently depends on whether accessory spleens have been found and removed. In the event of recurrence of symptoms, especially in thrombocytopenic purpura, "the uncertainty of finding splenic tissue at (the second) operation makes a surgical procedure prohibitively dangerous." In this series, accessory spleens were found and extirpated in 25 cases, or 18%. The two hypersplenic conditions for which splenectomy was most valuable were congenital hemolytic icterus and primary thrombocytopenic purpura. In about half of the cases of acquired hemolytic anemia of the primary type, splenectomy produced sustained remissions. Splenectomy is justifiable as a diagnostic measure in the presence of splenomegaly when agnogenic myeloid metaplasia has been excluded by bone marrow studies. Greater emphasis on preoperative bone marrow studies will clarify the indications for, and contraindications to, operative intervention. The discouraging results of splenectomy for congestive splenomegaly should stimulate further investigation for a procedure of curative value.

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Concentration of Folic Acid in Leukocytes: Observations on Normal Subjects and Persons with Leukemia. M. E. Swendseid, F. H. Bethell and O. D. Bird.—p. 864.
Nitrogen Mustard Inhibition of Azo Dye Carcinogenesis. A. C. Griffin, E. L. Brandt and V. Setter.—p. 868.
Use of X-Ray and Nitrogen Mustard to Determine Mitotic and Intermitotic Times in Normal and Malignant Rat Tissues. W. R. Widner, J. B. Storer and C. C. Lushbaugh.—p. 877.
Distribution of Radioactivity in Mice Following Administration of 3,4-Benzpyrene-5-C^{14} and 1,2,5,6-Dibenzanthracene-9,10-C^{14}. C. Heidelberger and S. M. Weiss.—p. 885.

Circulation, New York

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Heart Disease Case Finding by Means of 70 Millimeter Photofluorographic Films: Group I. D. D. Rutstein, C. R. Williamson and F. E. Moore.—p. 641.
Id.: Group II. C. R. Williamson, F. E. Moore and D. D. Rutstein. —p. 652.
*Screening Tests in Mass Surveys and Their Use in Heart Disease Case Finding. D. D. Rutstein.—p. 659.
Blood Lipids and Human Atherosclerosis: II. Influence of Heparin upon Lipoprotein Metabolism. D. M. Graham, T. P. Lyon, J. W. Gofman and others.—p. 666.
Effect of Small Doses of Heparin in Increasing Translucence of Plasma During Alimentary Lipemia: Studies in Normal Persons and Patients Having Atherosclerosis. W. J. Block, N. W. Barker and F. D. Mann. —p. 674.
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Regional Vasomotor Tone in Normotensive and Hypertensive Dogs. A. H. Williams and H. A. Schroeder.—p. 706.
Physiologic and Physical Factors that Govern Clinical Appreciation of Cardiac Thrills. T. B. Counihan, M. B. Rappaport and H. B. Sprague. —p. 716.
Action of Several Cardiac Glycosides on Conduction Velocity and Ventricular Excitability in Dog Heart. G. K. Moe and R. Méndez.—p. 729.
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Experimental Arterial Disease: I. Reaction of Pulmonary Artery to Minute Emboli of Blood Clot. W. B. Wartman, R. B. Jennings and B. Hudson. —p. 747.
Id.: II. Reaction of Pulmonary Artery to Emboli of Filter Paper Fibers. W. B. Wartman, B. Hudson and R. B. Jennings.—p. 756.
Management of Acute Cardiac Emergencies. C. E. de la Chapelle and O. A. Rose.—p. 764.

Screening Tests in Heart Disease Case Finding.—This paper discusses principles of screening tests for case finding in the general population and evaluates heart disease case finding studies carried out in Boston. The making of a 70 mm. photofluorographic film used in the Boston heart disease studies is a standardized procedure that can be performed by average technicians. One unsolved problem is the exposure of the film at a specific phase of the respiratory cycle to avoid fluctuations in heart size

due to changes in intrathoracic pressure during respiration. In order to be valid, a screening test must separate the "true positives" from the "true negatives," and keep to a minimum the number of "false positives" and "false negatives." The majority of those whose films were read as abnormal and who returned for examination had clinically significant heart disease. Thus the number of false positives does not invalidate the practicability of the 70 mm. photofluorographic film as a heart disease case finding procedure. On the other hand, the percentage of false negatives is unknown, because funds for the Boston studies did not provide for follow-up of a sample of those whose films were read as negative. Thus the ratio of false negatives to all negatives could not be calculated. The yield of previously unknown cases discovered and benefited in the Boston surveys was satisfactory, in comparison with yields usually obtained in mass surveys for other diseases. Patient acceptance of the case finding program was evidenced by the return for diagnosis of over three-fourths of those whose films were read as abnormal. However, this high rate of return required concerted follow-up efforts.

Diseases of Chest, Chicago

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Influence of Cortisone on Experimental Tuberculosis of Guinea Pigs. A. G. Karlson and J. H. Gainer.—p. 469.
Reversible Forms of Heart Disease. J. F. Briggs.—p. 482.
Oleothorax Following Pulmonary Resection. N. C. Andrews, D. R. Morton, G. M. Curtis and K. P. Klassen.—p. 501.
*Artificial Pneumoperitoneum in Treatment of Pulmonary Tuberculosis. J. L. Elliott and E. Blair.—p. 520.
*Treatment of Unusual Pulmonary Amebic Abscess with Chloroquine. A. E. Lindsay, W. H. Gossard and J. S. Chapman.—p. 533.
Use of Streptomycin in Tuberculosis and Pregnancy: Case Report. A. Froman.—p. 539.
Tuberculosis in General Hospitals: Need for Control Program. S. Jacobs. —p. 545.
Tuberculosis Patient in General Hospital. J. S. Edlin, S. Bassin and A. A. Richman.—p. 551.
Practical Use of Isolation Ward in General Hospital for Treatment of Tuberculosis. R. E. Neff.—p. 557.

Pneumoperitoneum for Pulmonary Tuberculosis.—The literature, mode of action, and method of induction of pneumoperitoneum for pulmonary tuberculosis are reviewed, and 70 cases are analyzed in which this treatment was used. It was found that pneumoperitoneum is a valuable adjunct in the therapy of pulmonary tuberculosis. It can be used alone or with phrenicectomy or phrenic crush. It is a relatively safe procedure, complications being comparatively rare.

Chloroquine for Pulmonary Amebic Abscess.—A case is reported of a man, aged 54, who had been in good health until about four months prior to hospitalization for a prolonged pulmonary infection. During the first three weeks in the hospital he was asymptomatic except for a cough productive of about one oz. (30 cc.) of green purulent sputum daily. Bronchoscopy revealed no evidence of bronchogenic carcinoma, and the bronchial secretions aspirated contained neither tumor cells nor acid-fast bacilli. Subsequently his temperature spiked to 102.4 F, malaise and anorexia became marked, and the liver became larger and tender. The white blood cell count rose, and the sputum became rusty brown. The following day motile trophozoites of Endameba histolytica were found in the sputum. Examinations of feces revealed no amebas. Emetine, 1 grain (60 mg.), daily for 10 days, but at the end of this time there was no appreciable change. The sputum remained positive for trophozoites, and the chest roentgenogram was unchanged. Chloroquine was started in doses of 1 gm. daily for two days followed by 0.5 gm. daily for 18 days. Procaine penicillin, 600,000 units daily, was also given to control possible secondary infection. One week after the institution of chloroquine therapy, cough was minimal and the sputum no longer rusty. After 10 days of chloroquine therapy, amebas disappeared from the sputum, and there was demonstrable roentgenographic improvement. It is suggested that the pulmonary amebic abscess resulted from hematogenous spread of amebic parasites from liver to lung. Since emetine alone failed to cause a satisfactory response, and chloroquine induced complete clinical remission, it is felt that chloroquine is a useful agent in pleuropulmonary amebiasis.

Endocrinology, Springfield, Ill.

49:429-564 (Oct.) 1951. **Partial Index**

Bioassay of Estrogens Using Mouse Uterine Response. B. L. Rubin, A. S. Dorfman, L. Black and R. I. Dorfman.—p. 429.
Metabolism of Steroid Hormones, Metabolism of Progesterone and Related Steroids. F. Ungar, R. I. Dorfman, R. M. Stecher and P. J. Vignos Jr.—p. 440.
Effect of Physiological Amounts of Estrogen on Secretion of Follicle Stimulating and Luteinizing Hormones. W. W. Byrnes and R. K. Meyer.—p. 449.
Metabolism of Intravenous Testosterone by Experimental Animals. C. D. West.—p. 467.
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"Panendocrinectomy" and Serum Proteins in Dog. R. Baker and G. H. Miller Jr.—p. 484.
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Relation of Adrenal to Blood Formation in Rat. A. S. Gordon, S. J. Piliero and D. Landau.—p. 497.
Immediate Kidney Response to Acute Stress. P. Constantinides.—p. 512.
Development of Obesity in Force Fed Young Thyroidectomized Rats. R. O. Scow.—p. 522.
Quantitative Inhibition of Progesterone by Estrogens in Development of Deciduomata. J. T. Velardo and F. L. Hisaw.—p. 530.
Response of Thyroid Gland of Rat to Severe Stress. R. Bogoroch and P. Timiras.—p. 548.

Florida Medical Association Journal, Jacksonville

38:307-378 (Nov.) 1951

Cerebral Arteriography: Its Use in Localization and Diagnosis of Intracranial Lesions. M. M. Greenfield and C. Keedy.—p. 323.
Treatment of Urinary Frequency in Women. J. C. Hayward, L. M. Orr II and J. B. Glanton.—p. 327.
Malignant Disease During Pregnancy. H. L. Harrell.—p. 330.
Fundamentals and Experiences in Use of Refrigerated Homogenous Bone. W. J. Newcomb.—p. 333.
Some Thoughts for a School Health Program. G. L. Beaumont.—p. 338.

Gastroenterology, Baltimore

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President's Address: Teaching and Research in Field of Gastroenterology. J. G. Mateer.—p. 191.
Clinical Evaluation of Caffeine Gastric Analysis in Duodenal Ulcer Patients. J. L. A. Roth.—p. 199.
*Late Effects on Gastric Acidity of Subtotal Gastrectomy for Gastric and Duodenal Ulcer. A. Cornell and L. Druckerman.—p. 216.
Delayed Excretion of Water with Regular Nocturnal Diuresis in Patients with Nontropical Sprue (Idiopathic Steatorrhea). E. E. Wollaeger and B. H. Scribner.—p. 224.
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Comparison of Effects of Methantheline Bromide (Banthine) and Atropine on Secretory Responses of Vagally Innervated and Vagally Denervated Gastric Pouches. C. F. Code, N. C. Hightower Jr. and G. A. Hallenbeck.—p. 254.
*Therapeutic Value of Banthine in Gastrointestinal Disorders. F. E. McDonough and P. B. O'Neil.—p. 265.
Abdominal Masses. IV. Diseases of Genito-Urinary System: Tumors of Kidneys, Carcinoma of Prostrate, Ovarian Tumors, Ovarian Cysts, Tubo-Ovarian Abscess, and Uterine Fibromyoma. D. B. Butler and J. A. Bargen.—p. 283.
Abdominal Masses. V. Systemic Diseases and Diseases of Special Regions: Chronic Myelogenous Leukemia, Chronic Lymphatic Leukemia, Lymphosarcoma, Polycythemia Vera, Tumors of Abdominal Wall, and Retroperitoneal Tumors. D. B. Butler and J. A. Bargen.—p. 303.
Bacitracin Therapy in Chronic Bacillary Dysentery. D. N. Silverman. —p. 320.
Determination of Proteolytic Enzymes and Proenzymes in Human Pancreatic Juice. W. Troll and H. Doubilet.—p. 326.
Observations on Effect of Orally Administered Atropine on Gastric Response to Insulin in Patients with Duodenal Ulcer. B. F. Gill. —p. 331.
*Role of Resins in Treatment of Water Retention Associated with Cirrhosis of Liver. R. H. Moser, B. D. Rosenak, R. D. Pickett and C. Fisch.—p. 336.

Subtotal Gastrectomy: Effects on Gastric Acidity.—Subtotal gastrectomy is the preferred treatment for intractable peptic ulcer, because it produces a reduction in acidity or an achlorhydria. Widely differing postoperative acid figures have been reported, because as a rule only single determinations were made just before discharge from the hospital. This investigation was undertaken to determine the late acid values. One or more Rehfuss test meals were made on 154 patients three or more months after operation. This number included 114 patients with duodenal and 40 with gastric ulcers. In many reported series, gastric

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and duodenal ulcer are grouped together. This is incorrect because physiologically these two conditions are different and their therapeutic response to gastrectomy is not the same. In 40 cases of gastric ulcer, postoperative achlorhydria developed in 36 (90%). In four cases in which acid was present, achlorhydria was shown in three with a gruel test meal, but responded to histamine. If gruel alone had been employed, gastrectomy for gastric ulcer would have resulted in achlorhydria in 97% of the cases. Of the 114 patients with duodenal ulcer only 63 (55%) had postoperative achlorhydria. Of the 51 duodenal ulcer patients, who retained free acidity postoperatively, 9 had unsatisfactory results, 4 had jejunal ulcer, and 5 had other complications producing massive gastrointestinal hemorrhage. Reoperation was required in four of these patients.

Methantheline Bromide in Gastrointestinal Disorders.—Methantheline bromide (banthine®), through an anticholinergic action similar to that of atropine, decreases gastric motility, delays gastric emptying, and diminishes peristalsis in the small bowel and colon. McDonough and O'Neil of the Lahey Clinic gave 100 to 400 mg. of methantheline bromide daily in divided doses along with routine treatment to 170 patients with peptic ulcer or other gastrointestinal disorders characterized by hypermotility or hypersecretion, or both. As a result, four patients with acute duodenal ulcer were promptly benefited, and their ulcer healed. Fifty-nine of 100 patients with chronic recurrent duodenal ulcer were symptomatically relieved and did not have a recurrence when one could be expected according to their previous history. An additional 10% of the patients, although they had a recurrence, are continuing methantheline therapy, because it lessened either the frequency or severity of their recurrences. All three patients with jejunal ulcer were relieved and their ulcer healed. Two of four patients with gastric ulcer failed to respond favorably. Three of six patients with hyperchlorhydria, three of five patients with hypertrophic gastric rugae, and three of four patients with hiatus hernia were not benefited. Seven of 10 patients with resection of from 7 to 300 cm. of ileum and of the right colon, with ileotransverse colostomy, were symptomatically improved. One patient with a hyperfunctioning ileostomy was benefited, the other was not. Only 10 of 17 patients with the irritable colon syndrome were benefited. Two patients with the dumping syndrome were relieved. None of three patients with chronic relapsing pancreatitis was relieved of pain. Approximately 11% of the 170 patients were unable to continue taking methantheline because of undesirable reactions. The authors regard methantheline as a valuable addition to existing therapeutic methods for duodenal ulcer, but it does not supplant conventional therapy, and it will not always prevent complications, nor intractability. In disorders characterized by intestinal hypermotility, methantheline relieves symptoms if the hypermotility is not secondary to partial obstruction.

Resins for Water Retention in Cirrhosis of Liver.—Sodium retention is apparently an important factor in ascites and/or edema associated with cirrhosis of the liver, but restriction of sodium involves reduction of protein intake to a level that is incompatible with modern concepts of the therapy of liver disease. If it were possible to allow the patient to partake of a diet only moderately restricted in sodium and at the same time prevent absorption of sodium from the gastrointestinal tract, then the two principles of liver therapy would not be compromised. The sodium-removing resins may provide the answer to this problem. Consequently, Moser and associates investigated the effect of such resins in eight patients with cirrhosis, whose ascites did not respond to salt restriction and supplemental salt-poor protein in the diet. A mixture of resins was used containing 59% of a carboxylic acid type of cation exchanger in the hydrogen cycle, 29% of the potassium salt, and 12% of a weakly basic polyamine formaldehyde anion exchanger resin. In five of the patients the ascites was controlled by simultaneous administration of 30 to 50 gm. of resins and restriction of the sodium intake to 1.5 gm. per day. In the sixth patient a lowering of the plasma carbon dioxide content necessitated a reduction in the dose of resin to 40 gm. per day and in the salt intake to 1 gm. per day. Ascites was controlled in the hospital but recurred at home, presumably due to failure to restrict sodium intake properly. In the seventh patient control was possible with 50 gm. of resin and 3 gm. of sodium daily. The eighth patient was treated for only eight days, during which time the weight remained stationary. Significant sodium and potassium depletion occurred in one case, and potassium depletion in another. Symptoms of hypokalemia disappeared following administration of potassium salts. The authors feel that resins are an important tool for control of water and salt retention due to cirrhosis of the liver. However, this form of therapy is not without some hazard, in that acidosis or at least a diminution of the plasma content of carbon dioxide may occur.

Georgia Medical Association Journal, Atlanta

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Clinical Approach to Congenital Heart Disease. J. W. Hurst.—p. 451.
Rectal Bleeding. L. J. Rabhan.—p. 464.
*Cat-Scratch Disease. I. L. Bennett Jr. and J. T. Melton.—p. 466.
Coccidioidomycosis: Report of Case in Georgia. F. H. Stubbs and J. L. Dixon.—p. 469.
Freedom from Government. E. Hess.—p. 474.
Possible Atomic Bomb Effects Applied to Atlanta. C. E. Dowman.—p. 476.
Medical Aid Plan for Civil Defense Metropolitan Atlanta Area. C. Eberhart.—p. 481.

Cat-Scratch Disease.—A benign suppurative lymphadenitis occurring after cat scratches was described by French observers in 1950 and subsequently other reports appeared in the European and American literature. However, Foshay, who studied several (unreported) cases in Cincinnati in 1932, is credited with having first called this entity "cat-scratch fever." Bennett and Melton present histories of five patients with cat-scratch disease recently observed in Atlanta. This subacute suppurative lymphadenitis often, though not invariably, follows exposure to cats. Its occurrence following exposure to other animals, including birds, has been described, and there have been cases in which the pathogenic agent was apparently introduced by other minor traumata such as scratches by thorns. Local manifestations are adenopathy, bubo formation, and draining sinuses; the systemic manifestations are usually slight and transient. The disease is probably due to a virus, although no specific agent has been isolated. Pathologically the lesion consists of a granulomatous lymphadenitis with abscess formation. The diagnosis is established by skin testing with antigen prepared from aspirated pus. The course is benign but may be prolonged. Aureomycin and terramycin may be effective in therapy.

Illinois Medical Journal, Chicago

100:273-324 (Nov.) 1951

Diagnosis and Treatment of Meningitis. A. L. Hoyne.—p. 285.
Acute Appendicitis. P. Thorek.—p. 290.
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Evaluation of Five Years Experience with Continuous Caudal Anesthesia. C. Greenstein.—p. 305.
Radioactive Digitoxin. F. E. Kelsey.—p. 309.
Galactose Tolerance Test. A. Kraft and W. Wolf.—p. 311.
Bleeding from Unsupervised Use of Dicumarol. H. J. Levine and H. E. Ryan.—p. 314.

Journal of Bacteriology, Baltimore

62:519-676 (Nov.) 1951. **Partial Index**

Nonadaptive Nature of Change to Full Streptomycin Resistance in Escherichia Coli. H. B. Newcombe and J. McGregor.—p. 539.
*Chemically Defined Medium Suitable for Production of High Titer Diphtherial Toxin. R. M. Drew and J. H. Mueller.—p. 549.
Studies of Sulfur Metabolism of Brucella Suis. L. J. Rode, C. E. Lankford and V. T. Schuhardt.—p. 571.
Nutrition of Heterofermentative Lactobacilli that Cause Greening of Cured Meat Products. J. B. Evans and C. F. Niven Jr.—p. 599.
Allergenic Property of Scarlatinal Toxin. D. A. Boroff.—p. 627.
Further Observations on Zone Phenomenon in Bactericidal Action of Penicillin. H. Eagle.—p. 663.

Medium for Production of High Titer Diphtherial Toxin.—The amino acid requirements of Corynebacterium diphtheriae, Toronto strain of Park-Williams no. 8, were investigated. It was shown that excellent growth and toxin production can be obtained on a medium composed of eight amino acids, ammonium sulfate, trace metals, inorganic salts, four accessory growth fac-

tors, and maltose. The amino acids include glutamic acid, cystine, proline, tryptophan, leucine, valine, methionine, and glycine. Ammonia could be utilized as a partial source of nitrogen. Thiamine is an additional growth stimulatory factor for the Toronto strain because of its accelerating effect on the rate of growth and toxin-formation. The proposed medium compares favorably with casein hydrolysate medium in its capacity to support the production of high titer diphtherial toxin.

Journal of Immunology, Baltimore

67:379-448 (Nov.) 1951

High Intensity Electrons as Tool for Preparation of Vaccines: I. Preparation of Rabies Vaccine. F. B. Traub, U. Friedemann, A. Brasch and W. Huber.—p. 379.

Pig Complement and Its Fractionation for Production of Reagents Containing Third Component. J. Jonsen, W. Manski and M. Heidelberger. —p. 385.

In Vivo Stability of I^{131} Protein Label of Rabbit Antibody in Guinea Pigs as Determined by Quantitative Precipitin Reaction. L. R. Melcher and S. P. Masouredis.—p. 393.

Studies on Vaccinia Virus: I. Development of Hemagglutinating and Infective Particles in Chorioallantois of Chick Embryo. B. A. Briody and C. Stannard.—p. 403.

Id.: Neutralization of Vaccinia Virus by Normal Guinea Pig Serum. B. A. Briody, N. Ledinko and C. Stannard.—p. 413.

Effect of Proflavine on Growth of Viruses in Chick Embryo. B. A. Briody and C. Stannard.—p. 423.

Mouse-Egg Neutralization: Neutralization in Mouse of Influenza Viruses Not Adapted to Mouse. E. D. Kilbourne and F. L. Horsfall Jr.—p. 431.

Comparison by Means of Complement-Fixation Test of Relative Potencies of Chloramphenicol, Aureomycin, and Terramycin in Experimental Q Fever Infections in Embryonated Eggs. R. A. Ormsbee and E. G. Pickens.—p. 437.

Journal-Lancet, Minneapolis

71:473-514 (Nov.) 1951

Cortisone in Allergic Asthma. J. S. Blumenthal.—p. 473.

ACTH and Cortisone in Ophthalmology. J. P. Wendland.—p. 482.

Fatigue States Associated with Abnormal Carbohydrate Metabolism. G. A. Cronk.—p. 484.

Early Diagnosis of Malignant Lesions of Genito-Urinary System. B. C. Corbus Jr.—p. 488.

Difficulty in Removing T-Tubes from Bile Ducts. A. L. Cameron.—p. 491.

Problems in Management of Severe Diabetes. H. O. Mosenthal.—p. 493.

Digestive Tract in Medical Literature. J. A. Bargen.—p. 497.

Journal of Pediatrics, St. Louis

39:519-644 (Nov.) 1951

*Transmission of Poliomyelitis Virus: Analysis of Differing Interpretations and Concepts: Practical Implications. A. B. Sabin.—p. 519.

Various Aspects of Adolescence. J. R. Gallagher.—p. 532.

Aureomycin Treatment of Diphtheria and Diphtheria Carriers. S. Karelitz, H. King and I. S. Rubinstein.—p. 544.

*Treatment of Pertussis with Aureomycin, Chloramphenicol, and Terramycin. L. Weinstein, R. Seltser and C. T. Marrow III.—p. 549.

Citrovorum Factor in Leucemia: Two Cases with Autopsy Findings. A. M. Earle, W. A. Reilly and W. G. Lawson.—p. 560.

Nummular Eczema in Children: Report of Six Cases. H. H. Perlman, J. Gropen and P. Westfall.—p. 565.

Congenital Atresia of Bile Ducts Associated with Erythroblastosis Fetalis. J. T. McGeehan, J. B. Butchart and D. P. Walker.—p. 575.

Growth and Development of Infants Receiving Proprietary Preparation of Evaporated Milk with Dextri-Maltose and Vitamin D. L. H. Frost and R. L. Jackson.—p. 585.

Electrocardiographic Changes in Exchange Transfusions. J. E. Gustafson. —p. 593.

Hypothyroidism Following Thyroidectomy for Congenital Obstructive Goiter. N. Schifrin and E. S. Hurwitt.—p. 597.

Method Adapted for Determination of Urinary 17-Ketosteroids in Children: With Some Considerations of Interpretation. A. M. Bongiovanni. —p. 606.

Transmission of Poliomyelitis Virus.—The virus of poliomyelitis in man is found in the central nervous system and in the digestive tract. Tests of the infectivity of saliva and mouth spray have yielded negative results. Studies have indicated that pharyngeal secretions are neither a source of virus-laden droplets for aerial transmission of the infection nor a significant source of virus for contamination of the hands. Thus, there is no evidence that the virus is transmitted by the respiratory organs. Moreover, this hypothesis implies transmission by casual association with exposure to virus-laden droplets rather than by the intimate association that appears to be most important in transmission of poliomyelitis. The virus occurs in feces of patients and of healthy carriers. It has been detected in stools with a frequency of 70 to 90% during the first week of illness and about 50% during the third and fourth weeks. The virus may be transmitted by feces in intimate association and other ways. The commonest mode of infection is through the mouth; contaminated food and drinks are as important as contaminated fingers. The period of communicability cannot be limited to a few days after onset; it should be regarded as potential as long as the virus is present in the feces. The role of filth flies as transmission agents of stool-borne virus may be important under different circumstances and conditions. More virulent strains may be in circulation in a community during an epidemic period. Measures to combat filth flies and minimize contamination of food should be taken, and elementary rules of hygiene aiming to diminish the individual's chances of infection should be observed.

Aureomycin, Chloramphenicol, and Terramycin in Pertussis.—Antibiotics were given to 80 children with pertussis, without complications at time of admission. Aureomycin was given to 19 patients, of whom 13 were less than one year old; chloramphenicol was given to 36, of whom 16 were less than one year old; and terramycin was given to 25, of whom 14 were less than one year old. The drugs were administered orally in divided doses of 50 to 70 mg. per kilogram of body weight daily for 14 days. In very young children the drugs were given rectally in daily doses of 100 mg. per kilogram of body weight. Three injections of 20 cc. of human hyperimmune serum were given every 48 hours to 35 children less than one year of age. Results showed that aureomycin, chloramphenicol, and terramycin had little or no effect in reducing the incidence or severity of coughing in the paroxysmal phase of pertussis. Terramycin was the most efficient of the three drugs in eliminating H. pertussis from the respiratory tract. Flora changes in the nasopharynx revealed the presence of some potentially pathogenic organisms that were not detected in the culture taken before the therapy and that became numerically significant after treatment was instituted. The number of complications due to secondary bacterial infections (bronchopneumonia, suppurative otitis, and monilial stomatitis) was lowest in patients treated with terramycin. In the aureomycin-treated children the incidence was greater than in untreated patients. Many of these infections were caused by bacteria that rarely induce complications in untreated cases. Terramycin is most effective in decreasing risks of complications and is the drug of choice when prophylaxis of secondary infection is attempted. The best treatment for pertussis is good nursing care, maintenance of adequate nutrition, hydration and electrolyte balance, and early and intensive treatment of complications.

J. Pharmacology & Exper. Therap., Baltimore

103:215-336 (Nov.) 1951. **Partial Index**

Toxicity Studies on Amberlite XE-96, Carboxylic Type Cation Exchange Resin. T. L. Flanagan, M. F. Sax and A. E. Heming.—p. 215.

Further Studies on (RC) Analogue of Acetylcholine and Some Additional Derivatives. F. W. Schueler and H. H. Keasling.—p. 222.

Comparative Actions of Analgesic, Hypnotic and Paralytic Agents on Hindlimb Reflexes in Chronic Spinal Dogs. R. W. Houde, A. Wikler and S. Irwin.—p. 243.

Some Actions of Procaine and Related Compounds on Dog's Auricle and A-V Connections. B. B. Brown and G. H. Acheson.—p. 269.

Effects of Synthetic Curare-Like Compound, Tri-Iodo Salt of Tris (Triethylaminoethoxy) 1, 2, 3 Benzene (Flaxedil), on Anesthetized Surgical Patient. B. E. Marbury, J. F. Artusio Jr., W. C. Wescoe and W. F. Riker Jr.—p. 280.

Comparative Pharmacology of Isomeric Nitrogen Methyl Substituted Heptylamines. D. F. Marsh, A. Howard and D. A. Herring.—p. 325.

Pharmacology of 1,1-Dimethyl-4-Phenylpiperazinium Iodide, Ganglion Stimulating Agent. G. Chen, R. Portman and A. Wickel.—p. 330.

Kansas Medical Society Journal, Topeka

52:473-524 (Oct.) 1951

Cerebrovascular Accident: Review of Some Pathological and Clinical Problems. A. T. Steegmann.—p. 473.

Cardiac Arrest with Successful Resuscitation. J. Tiller.—p. 480.

Diverticulitis of Sigmoid as Surgical Problem. E. S. Brinton.—p. 482.

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Michigan State Medical Society Journal, Lansing

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Diagnosis and Treatment of Chronic Diseases of Small Intestine. E. D. Kiefer.—p. 1258.

New England Journal of Medicine, Boston

245:671-710 (Nov. 1) 1951

"Two Centuries of Service—What of Next?" D. A. Clark.—p. 671.
Psychiatric Aspects of Cerebral Arteriosclerosis. E. B. Allen.—p. 677.
*Carcinoma of Cervix: Survival in 98 Cases Treated with Five-Day Radium Only. J. W. Bell, J. V. Meigs and C. H. Swan.—p. 684.
Mediterranean Anemia (Hereditary Leptocytosis) in a Chinese Family. J. H. Silverberg and D. Shotton.—p. 688.
Dental Decay and Its Control. P. K. Losch.—p. 690.

Carcinoma of Cervix Treated with Radium Only.—The records of 98 women who had received 6,000 milligram hours or more of radium for carcinoma of the cervix were carefully reviewed. Platinum needles containing 1, 2, and 3 mg. of radium were inserted circumferentially, the 3 mg. needle usually in the center of the growth and the 1 and 2 mg. needles on the periphery. The needles usually remained five days in situ, in some cases four days. A second dose of radium was used only for palliation or local recurrence. Three fourths of the patients had lesions described as either Stage 2 or 3. The radium treatment was designed chiefly for Stage 1 and 2 growths. It was realized that radium might be only a palliative measure in the treatment of Stage 3 and 4 neoplasms. The table listing the five-year survival rates indicates that of the 19 in Stage 1, 12 survived for five years or longer; of the 36 in Stage 2, 18 survived; of the 38 in Stage 3, 17 survived; and of the 5 in Stage 4, none survived. Thus of a total of 98 women with cervical cancer 47 survived more than five years. After 10 years 15 of the women were alive and well. Many observers feel that the average dose of 7,200 milligram hours is too large for women with Stage 1 and 2 lesions, causing unnecessary complications. Severe pelvic radiation reaction occurred in five patients, leading to development of a recto-vaginal fistula in four patients and to vesicovaginal fistula in one. Pyometrium occurred in one patient and pelvic or retroperitoneal hematomas in three. Two patients died of radiation ileitis with perforation and peritonitis. Intestinal obstruction necessitated laparotomy in two patients. At follow-up examinations 17 patients had considerable postradiation fibrosis and thickening in the broad ligament. Delayed radiation reaction (after three and five years) occurred in two patients. Postradiation complications of the urinary tract numbered 18 in all and included hydronephrosis, ureteral obstruction, radiation cystitis, incontinence, pyelonephritis, and uremia.

New Jersey Medical Society Journal, Trenton

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Oil Embolism Complicating Hysterosalpingography. N. Karshmer and W. Stein.—p. 496.
Primary Splenic Neutropenia. S. Friedenberg and R. S. Cotton Jr. —p. 497.
Diagnosis of Cancer of Esophagus and Stomach. J. E. Berk.—p. 501.
X-Ray Department in Civilian Catastrophes. E. F. Klein and B. Coplеman.—p. 505.
Eosinopenia in Status Asthmaticus: Report of Two Cases. P. B. Jennings. —p. 507.
Trimeton Maleate in Allergic Eye Manifestations. E. Kahan and G. Z. Carter.—p. 516.
Avitaminosis and Respiratory Moniliasis. R. A. Hall.—p. 512.
Epiphrenic Esophageal Diverticulum: With Report of Case. F. A. Marshall.—p. 513.
Treatment of Acute Subacromial Bursitis. H. Merliss.—p. 515.
Treatment of Trichinosis with Cortisone. F. Rothenberg.—p. 517.

New York State Journal of Medicine, New York

51:2439-2550 (Nov. 1) 1951

Clinical Value of Uterosalpingography. H. G. LaForge.—p. 2475.
Inversion of Puerperal Uterus. D. C. McGill and E. R. Dugan.—p. 2481.
Myomas in Pregnancy. R. J. Lowrie and K. Rosenberg.—p. 2485.
Value of Endometrial Curettage in Diagnosis and Treatment of Functional Uterine Bleeding. E. S. Taylor and J. C. Lombardi.—p. 2488.
Ectopic Pregnancy as Cause of Maternal Mortality in Brooklyn. A. H. Rosenthal and M. Glass.—p. 2493.
Anesthesia in Cesarean Section. H. S. Acken Jr., R. Waelsch and J. H. Ray III.—p. 2499.
*Cortisone in Allergic Purpura of Children. I. N. Kugelmass.—p. 2504.
Mesothelioma of Peritoneum. J. Rosenthal and M. Connor.—p. 2507.
Toxic Hepatitis Caused by Prolonged Inorganic Arsenic Intake: Studies on Liver Dysfunction—VII. L. Plener and S. Waldman.—p. 2511.
Nonpenetrating Injuries of Chest. W. W. Heroy and F. C. Eggleston. —p. 2515.
Acceleration of Blood Transfusions with Intravenous Procaine. N. Neustrup and J. Milowsky.—p. 2520.
Diagnostic Value of Liver Punch Biopsy. W. Aronson, J. C. Di Lorenzo and E. Katz.—p. 2523.

Cortisone in Allergic Purpura.—Allergic purpura with or without thrombocytopenia is usually accompanied by other allergic manifestations such as urticaria, angioneurotic edema, asthma, lymphadenopathy, arthritis, fever, and leukocytosis. When allergens are numerous and damage to the capillary endothelium widespread, repair of vascular injury may require weeks or months. With cortisone purpuric bleeding can be arrested in hours or days instead of weeks or months whether or not the offending allergens are eliminated. The author presents the histories of four children with allergic purpura who responded to treatment with cortisone. Two children with thrombocytopenia responded promptly to cortisone following a rapid increase of blood platelets and return to normal levels within a week. In the Henoch type of allergic purpura gastrointestinal disturbances cleared within 36 hours, purpuric manifestations within 48 hours, capillary fragility within 72 hours, and blood in urine and stools in 84 hours. In the Schönlein type of allergic purpura appetite improved promptly, fever dropped in 24 hours, joint pains disappeared in 48 hours, purpura faded in 96 hours, and the sedimentation rate was normal in five days. Mild manifestations of allergic purpura remained for weeks after the withdrawal of cortisone.

Northwest Medicine, Seattle

50:825-908 (Nov.) 1951

*Poliomyelitis in Adults in Seattle in 1949. J. L. Bakke and J. W. Haviland.—p. 846.
Effect of Pregnancy on Mortality Rate of Tuberculous Woman. N. P. Murphy.—p. 851.
Pleomorphic Adenoma and Adenocarcinoma of Parotid Gland. W. J. Sinclair.—p. 852.

Poliomyelitis in Adults.—Sixty cases of poliomyelitis in adults observed in one hospital in Seattle during one season are reviewed, and it is assumed that they are representative of the cases observed over the entire state. Three of the 60 patients died of poliomyelitis, a mortality of 5%, which is consistent with the mortality of 5.9% reported for 235 patients over 13 years of age in the entire state during this period. All three deaths occurred in men with bulbar involvement. There were 32 men and 28 women. Of the men, 27 had paralysis, but only 15 of the women had paralysis; 16 of the 23 patients with bulbar involvement were men. Comparing these figures with those for the entire state, it was found that the age and sex distribution of the cases reviewed here was normal. It is the general consensus that the incidence of poliomyelitis in pregnant women is greater than in the general population, and that they are more susceptible to bulbar paralysis. In this series there were 11 female patients over 15 years of age with the paralytic type of poliomyelitis. Three of these were pregnant at three, six, and seven months, respectively, and all three had bulbar paralysis. History of a prodrome is much less frequent among adults than among children. The electrocardiograms of 3 of 13 patients showed abnormal function. Attempts to isolate poliomyelitis virus from fresh myocardium of a fatal case with clinical evidence of myocarditis were unsuccessful. Tracheotomy is an important adjunct in treatment of bulbar cases, but it should not be done routinely. Predominance of palsy in dominant limbs was noted and is offered as evidence for the fatigue theory of paralytic involvement.

Radiology, Syracuse, N. Y.

57:477-628 (Oct.) 1951

Dural Sinus Venography. B. S. Ray, H. S. Dunbar and C. T. Dotter. —p. 477.
Cerebral Arteriography in General Hospital Practice. R. C. Moore. —p. 487.
*Diagnosis of Complete Transposition of Great Vessels. H. L. Abrams, H. S. Kaplan and A. Purdy.—p. 500.
*Asymptomatic Gastric Mucosal Prolapse. E. J. Levin and B. Felson. —p. 514.
Rupture of Spleen: Roentgen Diagnosis. J. Gershon-Cohen, M. B. Hermel, R. N. Byrne and L. S. Bringhurst.—p. 521.
Combined Radiation Therapy and Surgical Treatment of Technically Inoperable Cancer. G. T. Pack and T. R. Miller.—p. 529.
Use of ACTH and Cortisone in Treatment of Post-Irradiation Pulmonary Reaction. S. W. Cosgriff and M. M. Kligerman.—p. 536.
Olfactory Esthesioneuro-Epithelíomas. W. B. Seaman.—p. 541.
Chondroangiopathia Calcarea seu Punctata: Review and Case Report. E. R. Haynes and W. F. Wangner.—p. 547.
Clinical and Roentgen Observations of Newly Perforated Peptic Ulcer. A. J. Winham and G. R. Pechstein.—p. 551.
Fictitious Pelvic Mass. S. L. Beranbaum.—p. 554.
The Johns Hopkins Fluoroscopic Screen Intensifier. R. H. Morgan and R. E. Sturm.—p. 556.
Effect of Single Massive Doses of Roentgen Radiation upon Liver: Experimental Study. I. M. Ariel.—p. 561.

Diagnosis of Complete Transposition of Great Vessels.—This is a report of 10 cases of transposition of the great vessels, 9 proved by autopsy and 1 by angiocardiography. The data on these cases were compared with those of 150 cases collected from the literature. The aim was to amplify and clarify the criteria for diagnosis. Transposition of the great vessels is much more frequent in males than in females and few of the children reach the age of 5 years. An enlarged right ventricle was one of the common denominators of most of the reported cases for which adequate autopsy data were available. In some patients the right auricle was enlarged, and the left ventricle was frequently enlarged. Associated shunts, such as patent ductus arteriosus, patent foramen ovale, interauricular septal defect, or interventricular septal defect, were nearly always present. The most frequent clinical findings in the reported cases were early severe cyanosis, with associated dyspnea, clubbing, and polycythemia; cardiac enlargement; variable murmurs, usually systolic; and right axis deviation. Studies on their own cases convinced the authors that the cyanosis is usually uniform in distribution; murmurs and their intensity and transmission depend on the shunts and the state of compensation; and arm and leg pulses are usually normal. The most important roentgenologic signs of transposition of the great vessels are increased heart size, a cephalolateral bulge in the left midcardiac border, a narrow mediastinal shadow in the frontal projection, widening of the great vessel shadow in the left anterior oblique projection, prominence of the pulmonary arterial branches, and right and left ventricular enlargement. Both the clinical and the roentgenologic aspects of the transposition of the great vessels must be taken into consideration in differentiation from tricuspid atresia, the tetralogy of Fallot, the Eisenmenger complex, and the Taussig-Bing syndrome. The cardiac configuration in complete transposition of the great vessels is not pathognomonic. A similar appearance may be seen in cases of coarctation of the aorta of the infantile type, interventricular septal defect, and various types of acquired heart disease. The diagnostic value of the roentgenographic appearance of the heart lies in the fact that it is usually distinctly different from the appearance in the other common cyanotic congenital cardiac malformations.

Asymptomatic Gastric Prolapse.—Unquestionably, patients with prolapse of the gastric mucosa often have symptoms that have been relieved by various therapeutic measures, including diet, antacids, psychotherapy, and surgery. It has never been established, however, that the prolapse is actually the cause of these symptoms and not simply an incidental finding. The fact that Levin and Felson occasionally observed significant degrees of prolapse unassociated with gastrointestinal complaints increased their uncertainty and led them to determine the incidence in asymptomatic patients. They made roentgenologic studies on the upper gastrointestinal tract of 100 patients who had no gastrointestinal symptoms and observed prolapse of the gastric mucosa in 18 cases. The prolapse was slight in 10, moderate in 5 and severe in 3 of the patients. The authors feel that the clinical significance of gastric prolapse has been overemphasized, and that it is seldom the cause of symptoms.

Southern Medical Journal, Birmingham, Ala.

44:993-1088 (Nov.) 1951

*Hypercholesterolemia. A. McMahon, H. N. Allen, C. J. Weber and W. C. Missey Jr.—p. 993.
Supernumerary Ureter, Blind at Cephalic End, with Ectopic Opening into Anterior Urethra: Case Report. W. A. Farmer and J. Mendeloff. —p. 1002.
Volvulus of Colon. L. Rademaker and E. L. Royer.—p. 1005.
Medical Treatment of Peptic Ulcer. A. Weinstein.—p. 1008.
Surgical Treatment of Peptic Ulcer. R. M. Larsen.—p. 1016.
Clinical Features of Walled Off Perforated Peptic Ulcer: Analysis of 100 Cases. C. Cassel, J. M. Ruffin and F. C. Bone.—p. 1021.
Problem of Silent Gallstone. R. M. Moore, A. F. Kauffmann III and J. P. McNeill.—p. 1027.
Appraisal of ACTH and Cortisone as Therapeutic Agents. T. D. Spies, R. E. Stone, G. Garcia-Lopez and others.—p. 1034.
*Simple or Radical Mastectomy: Analysis of Cases. W. R. Deaton Jr. and H. H. Bradshaw.—p. 1042.
Management of Borderline Pelvis. W. E. Brown.—p. 1046.
Sterility. W. F. Mengert.—p. 1050.
Psychic Aspects of Sterility and Abortion. T. E. Mandy, E. Scher, R. Farkas and A. J. Mandy.—p. 1054.
Evaluation of Treatment of Thyroiditis. J. H. St. John and W. M. Nicholson.—p. 1059.
Conservative Management of Painful Shoulder. D. L. Rose.—p. 1063.
Thermal Allergy: Clinical Evaluation and Management. H. J. Rinkel. —p. 1067.
Xylocaine®: New Local Anesthetic Agent. O. B. Crawford, C. Brasher, P. Ottosen and W. W. Buckingham.—p. 1073.
Teaching of Social Medicine: Who Will Bell the Cat? H. A. Kemp. —p. 1076.

Hypercholesteremia.—In a general medical practice 822 unselected patients, including men and women from the second to the ninth decades of life, were studied for the purpose of establishing the relationship of blood cholesterol levels to age, sex, blood pressure, basal metabolism, and various disease states. Of the 822 patients, 554 showed no significant disease states known to be associated with a change in cholesterol values. They served as the "normal" group for the study. These patients were arranged in age groups by decades in an attempt to establish a practical norm with which the blood cholesterol level of any person might be compared. The sex differential was observed to be of no practical significance. Determination of blood cholesterol levels in the normal group revealed a range of the levels from 112 to 438 mg. per 100 cc. The mean average cholesterol level for all ages was 228 mg. per 100 cc., with a standard deviation of plus or minus 41.6. An analysis of the mean average cholesterol levels in the age groups revealed a progressive increase in values with advancing years to a point between the ages of 50 and 60, at a mean age of 53.7 years, and a decline in cholesterol values in the later decades. Individual blood cholesterol levels should be compared with the mean average blood cholesterol levels for the age groups in determining the normal status of a particular level. The 268 patients rejected from the normal group because of the presence of disease states, had blood cholesterol levels conforming to the levels reported in the literature for these diseases. Of these 268 patients, 142 classified as having myocardial disease presented an age-group curve similar in configuration to the "normal" age group curve. The increase in the mean average cholesterol levels in the former group with increasing age was comparable to the increased clinical incidence of the degenerative diseases in the older age groups. The presence of a high blood cholesterol level unexplained by an obvious disease requires more complete and prolonged study to establish the significance of the abnormality. A high cholesterol level may be considered an abnormal cholesterol level until proven otherwise.

Mastectomy in Carcinoma of the Breast.—Of 84 patients with microscopically proven cancer of the breast, 54 were treated by radical mastectomy, followed by x-ray therapy in those with axillary node metastases, while 30 patients were subjected to simple mastectomy followed by x-ray therapy. Of the patients with radical mastectomy, 24 are still alive, a survival rate of 44.4%, and six of those now dead lived longer than five years postoperatively, a five-year survival rate of 54.7%. Using Cade's modification of Portmann's original classification, the survival rate for patients with Stage 1 lesions was 81.2% (13 of 16); for Stage 2, 48.4% (16 of 33). None of the five patients with Stage 3 lesions lived as long as five years, and no patient with Stage 4 lesions was treated by radical mastectomy. These results compare favorably with those reported by other clinics. Of the 30 patients treated with simple mastectomy plus postoperative

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irradiation, 15 are now alive, a survival rate of 50%. Of the 15 dead, 4 lived longer than five years, a five-year survival rate of 63.3%. Simple mastectomy yielded a 91.6% (11 of 12) five-year survival rate for Stage 1, and a 77% (7 of 9) five-year survival rate for Stage 2 lesions. Patients with Stage 3 lesions had a survival rate of 16.7% (1 of 6) and none of the patients with Stage 4 lesions lived as long as five years. These results indicate that simple mastectomy offers a better prognosis than radical mastectomy. The authors admit that their series is quite small, but they believe that until larger series are available, the cumulative data from such small series must suffice for temporary evaluation of the McWhirter type of therapy.

Surgery, Gynecology and Obstetrics, Chicago

93:529-656 (Nov.) 1951

The Present Story on Battle Casualties from Korea: Six Months' Study. W. F. Bowers, F. T. Merchant and K. H. Judy.—p. 529.
Standard Contact Burn: Method of Production and Observation on Blood Picture Following Its Production in Dogs. J. W. Brooks, P. Robinett, T. L. Largen and E. I. Evans.—p. 543.
Ileostomy for Ulcerative Colitis: Technique, Complications, and Management. R. Warren and L. S. McKittrick.—p. 555.
Treatment of Edema of Arm. W. T. Foley.—p. 568.
*Chronic Thyroiditis: Supravital Studies of Surgical Goiter Specimens. V. E. Chesky, W. C. Dreese and C. A. Hellwig.—p. 575.
Evaluation of Preoperative Skin Preparation. J. J. Murphy, J. A. Dull, J. Gamble and others.—p. 581.
Aberrant Systemic Arteries to Lower Lung. F. H. Cole, F. H. Alley and R. S. Jones.—p. 589.
Rectocolic Anastomosis: Simplified Method. E. D. Sugarbaker and H. M. Wiley.—p. 597.
Method of Closing Defects in Bowel. E. J. Poth and R. G. Martin.—p. 606.
Ectocervix During Gestation. J. J. Nolan and O. J. Pollak.—p. 609.
Effect of Banthine, Vagotomy, and Subtotal Gastrectomy upon Pancreatic Secretion. J. R. Thistlethwaite.—616.
Pancreatic Injuries: Experimental Study. H. L. Popper and H. Necheles.—p. 621.
*Studies on Vagotomy in Treatment of Peptic Ulcer: V. Clinical and Physiologic Results Three to Four Years After Surgery. I. F. Stein Jr. and K. A. Meyer.—p. 625.
Major Surgery in Hodgkin's Disease. R. D. Williams, N. C. Andrews and R. P. Zanes Jr.—p. 636.

Chronic Thyroiditis.—During the last 10 years Chesky and associates observed 169 cases of chronic thyroiditis among 2,031 patients requiring thyroidectomy, an incidence of 8.3%. The 169 cases included 8 cases of Riedel's struma (fibroplastic form), 146 cases of Hashimoto's disease (lymphadenoid goiter), 9 cases of giant cell thyroiditis of DeQuervain, and 6 cases that could not be classified, representing the earliest stages of chronic thyroiditis. The authors present the results of their supravital studies that led to a new concept of the etiology of chronic thyroiditis. In most of the 54 goiters examined they found large cells containing coarse salmon-red granules in the cytoplasm. In 30 specimens these large cells were found within the lumen of follicles; in 18 goiters they were seen in the interfollicular tissue. These cells were macrophages, and to determine the significance of these macrophages the authors studied paraffin sections of thyroids showing chronic inflammation. On the basis of their investigations they stress the following points: 1. Small foci of chronic thyroiditis characterized by aggregations of lymphocytes are common in exophthalmic and nodular goiters (63.9%) and not infrequent in normal-sized thyroids obtained by autopsy (16.2%). 2. There are only quantitative differences between the severe grades of chronic thyroiditis (Riedel's, Hashimoto's, and DeQuervain's type) and localized foci of chronic thyroiditis in exophthalmic goiter and nodular goiter. 3. All attempts to find bacteria or a virus as the cause of chronic thyroiditis have been unsuccessful. 4. Supravital studies of fresh surgical material suggest a new concept of the cause of this disease. By change in the composition of colloid, macrophages are attracted that invade the lumen of follicles, ingest colloid, and return into the interfollicular stroma. If they disintegrate in the stroma the liberated colloid attracts lymphocytes that cluster around the colloid and produce the anatomical picture of chronic thyroiditis. Excess thyrotropic hormone seems the most important factor in the causation of the colloidal changes responsible for the attraction of the macrophages. 5. The new concept of chronic thyroiditis as a chemical inflammation—comparable to lipogranuloma—is supported by experimental, supravital, and electronmicroscopic findings.

Vagotomy in Peptic Ulcer: Late Results.—Two important questions remain to be answered before vagotomy can be evaluated finally. It must be ascertained (*1*) what proportion of patients operated on continue to have unpleasant symptoms or have a recurrence of ulcer symptoms after a number of years; (*2*) whether the marked decrease in gastric secretory capacity and motility found in the early postoperative period is permanent. A total of 40 patients were followed for from 28 to 50 months. The clinical results in these 40 patients were good in 26, fair in 10, and poor in 4. The patients were subjected to physiologic tests and three types of response are differentiated: (*1*) normal vagus function, (*2*) partial vagus function, and (*3*) no vagus function. No significant change in the gastric secretory or motor activity is present in patients with normal vagus function following surgery. Reduction in the motility and in both spontaneous and stimulated acid secretion of the stomach is demonstrated in patients with partial vagus function and those with no vagus function three to four years after vagotomy. This reduction is greatest in patients with no vagus function. No evidence of any return of gastric activity is present in this group. A slight return of acidity is found in patients with partial vagus function as determined by the basal secretion; however, in spite of this, there is still a marked decrease in comparison with the preoperative level. The previous failure to recognize the existence of the intermediate group (partial vagus function) probably accounts for reports concerning the lack of correlation between the physiologic and therapeutic effects of vagotomy. The response of patients with partial vagus function to insulin hypoglycemia is delayed, and may be undetected unless observation is continued for at least two and a half hours after the injection of insulin. Spontaneous secretion of free hydrochloric acid during the night or basal secretion indicates vagus function. In addition, vagal type motility, either spontaneous or subsequent to hypoglycemia, indicates vagus function. Decrease in gastric motor and secretory activity following vagotomy in patients with partial vagus function and no vagus function remains three to four years after vagotomy.

Wisconsin Medical Journal, Madison

50:1065-1156 (Nov.) 1951

Essential Treatment of Major Burns. A. R. Mailer.—p. 1088.
Treatment of Vasospastic Conditions with Bentyl Hydrochloride: Preliminary Report. D. C. Ausman and J. J. Arneth.—p. 1089.
Effect of Ammonium Chloride on Clinical Pattern and Electroencephalogram in Epilepsy: Preliminary Report on New Addition to Therapeutic Armamentarium in Epilepsy. F. Kant and W. E. Gilson.—p. 1095.
Banthine in Treatment of Peptic Ulcer. J. Shaiken.—p. 1099.
Subtotal Gastrectomy: Analysis of 147 Consecutive Cases. W. M. Kearns Jr.—p. 1101.
*Silage Gas Poisoning: Case Report. G. A. Fostvedt.—p. 1103.

Silage Gas Poisoning.—The case is reported of a man who entered a previously closed silo. He cried for help, but a few minutes later was found in an unconscious state. Examination revealed arrhythmia, slow and shallow respiration, absence of reflexes, and occasional twitchings of the facial muscles. The patient did not respond to pain stimuli or the spoken voice. The pupils were dilated. The patient appeared to be anesthetized. He was given oxygen and respiratory stimulants, such as ammonia inhalations, injections of nikethamide (coramine®), camphor, and caffeine and sodium benzoate. Strophanthin was given for the cardiac embarrassment. Consciousness was restored after about one hour, but abdominal cramps persisted for another hour; arrhythmia persisted and he had a headache, but slept well the next night and felt well the following morning. He reported that he had become faint and had lost muscular coordination within one-half minute after climbing into the silo. The accidental anesthesia and toxic reactions presumably were due to carbon dioxide from silage fermentation. Carbon dioxide formation occurs also in beet sugar manufacture, yeast production, in wine vats, in linseed oil production, in brewery vats, and from dry ice. To prevent acute intoxication from silage gas, the silo area should be ventilated prior to entering it, and the atmosphere should be tested with a candle flame or a small animal, such as a bird or a mouse.

FOREIGN

Acta Chirurgica Scandinavica, Stockholm

102:167-240 (No. 3) 1951. **Partial Index**

Surgical Treatment of Wide Patent Ductus Arteriosus. P. Sandblom and G. Ekström.—p. 167.
*Double Aortic Arch. G. Ekström and P. Sandblom.—p. 183.
Post-Operative Changes in Circulation and Effects of Oxygen Therapy. L. Troell.—p. 203.
On Catgut Tetanus and Sterility of Catgut. T. Savolainen.—p. 215.

Double Aortic Arch.—A double aortic arch is reported in two girls, who were operated on at the age of 5 years and 2 months, respectively. Left thoracotomy with subperiosteal resection of the fourth rib, performed according to Crafoord's method in both cases, provided an excellent approach. In the older girl both arches were of the same diameter. The ligamentum arteriosum was cut and division of the left aortic arch and suture was performed according to Gross' technique. The postoperative course was uneventful and symptoms of compression or infection of the respiratory tract did not recur after the operation. In the second case, the diameter of the left arch was much smaller than that of the right. Division of the left arch was first carried out between double ligatures. The left subclavian artery also was divided, and only then did the posterior part of the left arch slip to the right behind the esophagus so that the vascular ring opened. Immediately after operation the patient had no respiratory symptoms, but laryngeal stridor reappeared within 12 hours, necessitating tracheotomy. A review is presented of 83 cases of double aortic arch reported in the literature. Of these 83 patients, 43 presented symptoms of compression from a vascular ring. Division of the compressing vascular ring, including division of the ligamentum arteriosum and ductus arteriosus, was adequate surgical treatment in 29 cases. There were six postoperative deaths. From their experience in two cases and data from the literature the authors draw the following conclusions: congenital respiratory stridor may suggest double aortic arch, and roentgenologic examination of the trachea and esophagus should be made with the aid of a water-soluble contrast medium such as 35% aqueous solution of iodopyracet ("umbradil"). Children with severe symptoms of compression not given surgical treatment usually die within the first seven months of life. Children with mild symptoms of compression may, despite continual pulmonary complications, occasionally survive with conservative treatment in the form of prophylaxis against infection and chemotherapy of bronchopneumonia. The ductus arteriosus should as a rule be approached from the left side. Right thoracotomy is preferred when preoperative roentgenograms reveal a left aortic knob and a large retroesophageal vessel. Double aortic arch with symptoms of tracheal obstruction from compression indicates surgical intervention. If symptoms are mild, operation may be postponed until the child is one-year-old. In the absence of compression surgical treatment is not indicated.

Annales Medicinae Internae Fenniae, Helsinki

40:99-196 (No. 2) 1951. **Partial Index**

Pulmonary Mycosis: Clinical and Pathological Features. R. Elo, R. Pätiälä and V. Ritama.—p. 99.
Essential Thrombocytopenia and Pregnancy: Report of Case. E. Helske.—p. 117.
Electrocardiographic Observations on 650 Finnish Athletes. E. Klemola.—p. 121.
Inflammatory Vascular Changes in Coronary Disease. V. Ritama, H. Laitinen and M. Virkkunen.—p. 133.
*Coarctation of Thoracic Aorta with Dissecting Aneurysm Distal to Obstruction: Review of Literature and Report of Case. E. Taipale and Per-Erik Heikel.—p. 187.

Coarctation of Thoracic Aorta with Aneurysm.—A study of the literature revealed 26 cases of coarctation of the aorta with associated aneurysm of the descending aorta distal to the obstruction. In 21 cases the patients died at an average age of 29 years, the cause of death being rupture of the aneurysm in 14. Three patients had borne children. A case is reported of a woman, aged 52, in whom coarctation of the aorta with an aneurysm distal to the obstruction was diagnosed during life. She had had two children. This patient died of myocardial infarction, and at autopsy a dissecting aneurysm was found. Histological examination showed marked calcification of the aortic aneurysm.

Annales Paediatrici, Basel

177:277-328 (Nov.) 1951

*Administration of PAS by the Lumbar Route in the Course of Combined Treatment of Tuberculous Meningitis. M. H. Beguin.—p. 277.
The Morgagni-Adams-Stokes Syndrome in Diphtheria. E. Hausmann.—p. 294.
Studies on the Concentration of Free Amino-Acids in Infants and Children. J. Ströder, H. Grunhofer and W. Engel.—p. 304.
Heredity in Infantile Type of Gaucher's Disease. E. Stransky and T. L. Conchu.—p. 319.

***p*-Aminosalicylic Acid in Tuberculous Meningitis.**—Combined treatment of tuberculous meningitis with streptomycin and *p*-aminosalicylic acid ("PAS") minimizes the development of bacilli resistant to streptomycin. Bacteriostatic action of the two is additive, making it possible to use streptomycin in nontoxic doses. *p*-Aminosalicylic acid given only by mouth enters the cerebrospinal fluid in quantities generally too small to be effective; the proportion required in vitro ranges between 25 γ and 300 γ per 100 cc. The concentration varies, depending apparently on the albumin content of the cerebrospinal fluid. Two methods of obtaining an adequate concentration have been employed: (*1*) intravenous infusion by continuous drip, making it possible to give 40 gm. daily without the digestive disturbances that arise when the adult dose of 14 gm. is exceeded in oral administration; and (*2*) combined *p*-aminosalicylic acid and streptomycin given intrathecally. The second method was used with certain modifications in 10 cases. The author gave streptomycin and *p*-aminosalicylic acid intrathecally, with dihydrostreptomycin intramuscularly and *p*-aminosalicylic acid orally. Results obtained (7 patients apparently cured and 1 improved) were better than with streptomycin alone or combined with the acid given orally. Tolerance for the combined medication was excellent. A 5% solution of *p*-aminosalicylic acid is isotonic and has a pH of about 7, so that irritation due to acid reaction need not be feared. Doses of 3 mg. per kilogram of body weight given intrathecally were resorbed in 24 hours to the extent of from 100 to 600 γ per cent. One injection a day sufficed, because contact with bacteriostatic doses for several hours daily will arrest multiplication of the tubercle bacillus. Lumbar intrathecal injections should be continued for about six months to prevent relapse. The action of streptomycin and *p*-aminosalicylic acid is bacteriostatic and not bactericidal; definitive cure is obtained only when an impassable barrier has been built up around the bacilli that survive in the inflammatory meningeal lesions. The following scheme of treatment is suggested: intrathecally—streptomycin, at first 2 mg. per kilogram of body weight, then 1 mg., and the sodium salt of *p*-aminosalicylic acid, 3 mg.; intramuscularly—dihydrostreptomycin, at first 40 mg. per kilogram of body weight, later 20 mg.; orally—*p*-aminosalicylic acid, 0.25 to 0.3 gm. Lumbar punctures are made daily for one month, three times a week for two months, twice a week for two months, and finally once a week for one month. The concentration of the acid in the cerebrospinal fluid should be determined regularly, 200 to 300 γ per 100 cc. after 24 hours being sufficient. The 5% solution of sodium salt of *p*-aminosalicylic acid and the streptomycin are diluted with a physiological solution up to 5 to 10 cc. and given in the same syringe. The concentration of the acid solution should not exceed 1% (10 mg. per cubic centimeter) when given intrathecally. Dosage is adapted to each child; the number of punctures may be increased or decreased. Disturbance of hearing does not follow this dosage.

Beiträge zur Klinik der Tuberkulose, Heidelberg

106:91-182 (No. 2) 1951. **Partial Index**

Clinical Considerations Concerning Treatment of Miliary Tuberculosis of Lungs and Tuberculous Meningitis with Streptomycin. H. Gaus and M.-L. Schikarski.—p. 93.
Absorption Increasing Effect of Hyaluronidase on Inhalation of Tuberculostatic Substances. A. Lass.—p. 104.
Preliminary Results of Chemotherapy of Pulmonary Tuberculosis with Respect to Transmission of Contagious Diseases. C. Göttsching.—p. 113.
*Inhalation Therapy with Antibiotic Substances. T. Lammers and K. Herold.—p. 158.

Inhalation Therapy with Antibiotic Substances.—Satisfactory results from inhalation therapy with antibiotics depend on use of a suitable nebulizer, maintenance of therapeutic concentrations of the drugs in the lung tissues over prolonged periods,

and knowledge of the sensitivity of the bacterial content of the sputum. Therapeutic concentrations were maintained in the lung tissues for at least four and nine hours when 100,000 and 500,000 units of penicillin G, in 5 cc. of distilled water, were administered by aerosol inhaler. Therapeutic concentrations of aureomycin, streptomycin, and terramycin were maintained in the lung tissues for 12 to 14 hours by the administration of 500 mg. of each of these antibiotics in aerosol form. Because of the rapid absorption of penicillin by the lung tissues a therapeutic level of this antibiotic was maintained in the blood for three to four hours after inhalation of 100,000 units of penicillin and for seven to nine hours after inhalation of 500,000 units of penicillin. Streptomycin, aureomycin, and terramycin were absorbed by the lung tissues more slowly and in smaller amounts than penicillin, and therapeutically effective blood levels were not obtained when these antibiotics were administered by inhalation. The plasma concentration of penicillin was increased and its duration in the plasma was shortened by the addition of isopropylarterenol ("aludrine") to the aerosol. Hyaluronidase added to the aerosols caused liquefaction of necrotic lung tissue without impairing absorption of antibiotics. A pronounced decrease of bacteria in the sputum resulted from inhalation of the antibiotics. With prolonged penicillin inhalation therapy the number of penicillin-resistant bacteria (particularly coliform bacteria and yeasts) in the sputum increased. After two to three weeks of streptomycin aerosol treatment the same number of saprophytic bacteria were observed in the sputum following an initial reduction as had been observed previously, but all types of bacteria had become completely resistant to the usual therapeutically effective concentrations of streptomycin. The number of bacteria in the sputum remained low, even with prolonged terramycin and aureomycin inhalation therapy, and the bacteria in the sputum did not become resistant to these antibiotics.

British Journal of Dermatology, London

63:343-388 (Oct.) 1951

Association of Generalized Erythrodermia with Superficial Lymphadenopathy (Lipomelanic Reticulosis). A. Jarrett and H. S. Kellett.—p. 343.

63:389-430 (Nov.) 1951

Congenital Syphilis in One of Twins. T. James.—p. 389.
Case of Sarcoidosis with Erythrodermic Lesions: Treatment with Calciferol. J. E. M. Wigley and L. A. Musso.—p. 398.

British Journal of Ophthalmology, London

35:509-572 (Sept.) 1951

Diagnosis and Management of Paralysis of Extrinsic Ocular Muscles: With Special Reference to Surgical Treatment in 219 Cases. T. K. Lyle and A. G. Cross.—p. 511.
Aureomycin in Trachoma. J. W. R. Sarkies.—p. 549.
Electron-Microscopic Study of Infective Agent of Trachoma. Y. Itô, T. Itô and Y. Sasaki.—p. 553.
Retinal Micro-Aneurysms in Connection with Generalized Diseases Causing Retinopathy. R. Sysi.—p. 560.

British Medical Journal, London

2:1167-1232 (Nov. 17) 1951

Experimental Approach to Problem of Diabetes Mellitus. F. G. Young.—p. 1167.
Hyaluronidase Skin Spreading Effect: Analysis of Repeated Measurements. E. J. Holborow and M. K. Keech.—p. 1173.
Reconstitution of Dermal Barrier to Dye Spread After Hyaluronidase Injection. E. G. L. Bywaters, E. J. Holborow and M. K. Keech.—p. 1178.
*Eosinopenic Response to Cortisone and A.C.T.H. in Normal Subjects. J. H. Kellgren and O. Janus.—p. 1183.
Eosinophil Counting: Modification of Pilot's Method. J. C. W. MacFarlane and G. W. Cecil.—p. 1187.
Addison's Disease with Associated Polyarthritis: Aetiological Study of Arthritis Syndrome. J. E. Caughey and J. E. McCoy.—p. 1189.
*Penicillin Treatment of Acute Mastoiditis in Children. J. I. M. Black.—p. 1191.
Case of Myxoedema Developing During *p*-Aminosalicylic Acid Therapy. G. M. Komrower.—p. 1193.
Sign for Differentiating Uterine from Extrauterine Complications of Pregnancy and Puerperium. N. Alders.—p. 1194.

Eosinopenic Response to Cortisone and Corticotropin.—The eosinopenic responses to single doses of 6.25, 12.5, 25, 50, and 100 mg. of cortisone given orally and to single doses of 2.5, 5, 10, 20, 40 and 100 mg. of corticotropin (ACTH) given intramuscularly were studied in four normal men between the ages of 32 and 43. A modification of Dunger's technique was used for estimating the number of circulating eosinophils. Results showed that the time relations of the responses to these two drugs were remarkably similar, but the individual responses to either cortisone or corticotropin, or both, varied considerably. The eosinopenic response to various corticotropin preparations and to acute febrile stress induced by intravenous administration of 10 ml. of typhoid-paratyphoid (T. A. B.) vaccine were also compared, and throughout these studies the differences in individual responses were maintained. The number of circulating eosinophils was also studied during periods of stress from established panhypopituitarism in three patients who showed an exaggerated and prolonged eosinopenic response to cortisone given orally. Although many factors may influence eosinopenic responsiveness, it is suggested that the eosinopenic response of the individual to 50 mg. of cortisone administered orally, in addition to the corticotropin response test, might provide a useful guide to therapy with these hormones, and might indicate the activity of the pituitary-adrenal mechanism.

Penicillin in Acute Mastoiditis.—Of 118 children with acute mastoiditis treated with penicillin, 59 who did not have fluctuation recovered without surgical intervention. The remaining 59 patients had fluctuation, and in 38 of them the postauricular abscess had to be incised. In the other 21 the abscess was absorbed spontaneously. Only three patients required mastoidectomy, and one of them had tuberculous tympanomastoiditis. The dose of penicillin recommended is 300,000 units daily by intramuscular injection. Routine treatment of acute mastoiditis in children by penicillin injections is advocated. Once the penicillin treatment has been instituted, the patient should be examined daily. A rapid improvement in the general condition and temperature is to be expected. In a few days the postauricular swelling should show a reduction in size. When fluctuation is detected, if the abscess remains the same size for 24 hours it should be incised. If otorrhea is present and does not cease in about seven days, the pus should be examined for penicillin-resistant organisms, and appropriate action taken. Penicillin treatment should be continued until the tympanic membrane regains a normal texture and the tympanum contains air. All patients should be followed for about three months to be sure that hearing returns and that recovery is not retarded by factors such as enlarged tonsils and adenoids or sinusitis.

Edinburgh Medical Journal

58:457-520 (Oct.) 1951

*Survey of Granite Industry in Aberdeen with Reference to Silicosis. A. Mair.—p. 457.
Prognosis in Pulmonary Tuberculosis in Aberdeen and Aberdeenshire. R. Fraser.—p. 481.
Fatality and Survivorship in Pulmonary Tuberculosis: Study of Notified Cases in Edinburgh: 1936-44. M. S. Acker.—p. 489.
*Brochiectasis Treated with Chloramphenicol. N. Wynn-Williams and E. N. Moyes.—p. 503.
Lymphosarcoma Terminating with Leukaemia. W. R. Gauld.—p. 507.

Silicosis in the Granite Industry.—The dread of silicosis in the Aberdeen granite industry has made it difficult to obtain sufficient workers. Parents wished to prevent their boys learning a trade that, they believed, would cause early death from "mason's disease." Mair initiated this survey in 1948 in an attempt to determine the incidence of this disease in the industry. Of approximately 1,500 men working with granite, 521 were employed in some capacity involving a dust hazard, and 510 of these submitted to x-ray examination. Of these, 56 showed radiological evidence of silicosis. However, in 35 the silicosis was of a minor degree without other signs or symptoms. Silicosis severe enough to entitle the worker to receive disablement benefit was found in only 11. The mean ages of workers with four increasing degrees of silicosis (graded roentgenologically) were 53.7, 59.4, 63.2, and 65.4, respectively, while the corresponding mean "dust-years" necessary to produce these lung changes were 32, 38, 40, and 42. The findings in men at work and those retired, reveal that, while silicosis exists to a moderate extent, it commences so late in life and progresses so slowly that many stonecutters live

to comparative old age and die of other diseases. The incidence of tuberculosis in the men at work was found to be no higher than one would expect in the community at large. It is suggested that the high number of deaths among stonecutters in Aberdeen during the early part of the century registered as "phthisis" was actually due to tuberculosis and not to silicosis alone or silicosis complicated by tuberculosis.

Bronchiectasis Treated with Chloramphenicol.—The treatment of bronchiectasis with penicillin, by intramuscular injection and in the nebulized form, in some cases combined with streptomycin therapy, reduced the amount of sputum by an average of 61%. Since this treatment required hospitalization, Wynn-Williams and Moyes decided to try chloramphenicol administered by mouth, which had proved successful in treatment of three hospitalized patients with severe bronchiectasis. The authors chose 12 ambulatory patients for treatment with chloramphenicol either because they were known to have had sufficient sputum to have required previous treatment in the hospital, or because they stated their sputum was enough to cause inconvenience. Eight received treatment for five days, three had treatment for eight days, and in one the drug was stopped on the third day after only 7 gm. had been given because of side-effects. The sputum was reduced by an average of 83%, being entirely eliminated in four and rendered mucoid in eight. Compared with previous antibiotic treatment, chloramphenicol appeared to be more effective in four patients and equally effective in two. This result is noteworthy, since it was obtained in outpatients who continued normal activity. Probably the sputum will gradually increase, as following penicillin therapy, and some increase occurred in several patients within a few weeks. It is not claimed that chloramphenicol will remove permanently the infection in dilated bronchi, but, if these results can be repeated, a valuable antibiotic has been added to the therapeutic armamentarium.

Geburtshilfe und Frauenheilkunde, Stuttgart

11:771-866 (Sept.) 1951. **Partial Index**

Improvement in Irradiation Therapy in Advanced Cases and in Recurrences of Carcinoma of Cervix. R. K. Kepp.—p. 771.
*Incidence of Congenital Defects and Age of Mother. H. Hegnauer.—p. 777.
Intrauterine Death of Fetus and Toxoplasmosis. W. Dontenwill.—p. 792.
Cytologic Diagnosis of Primary Tubal Carcinoma from Vaginal Smear. G. Besserer.—p. 804.
Cytologic Findings in Cervical Smears in Presence of Endometritis and Tuberculous Cervicitis. H. Cramer.—p. 809.

Incidence of Congenital Defects and Age of Mother.—With data on 140,000 births, studies were made of the relationship between incidence of congenital deformities and age and parity of the mother. Women who gave birth between the ages of 36 and 40 had twice as many and those over 40 three times as many deformed children as did younger mothers. The incidence of developmental disturbances was higher with increasing numbers of pregnancies, but not as high as in relation with the age of the mother. Therefore it was concluded that the higher incidence in congenital deformities in this group was also the result of the higher age of the mother. The relation of incidence and age was not equal in all types of deformities. The incidence of defects in the extremities, genitalia, and facial clefts was not related to maternal age. However, defects in the central nervous system, such as mongolism, hydrocephalus congenitus, and anencephalus, showed a decided relation to the age of the mother, but surprisingly this was not true of deformities of the spinal cord. Studies of congenital goiter suggested that not only the mother's age but also the number of pregnancies determined the incidence.

Journal of Tropical Medicine and Hygiene, London

54:221-242 (Nov.) 1951

Assessment of Value of Cholera Vaccine as Used in Single Dose Mass Inoculation. L. Kant.—p. 223.
Toxoplamosis. E. W. Hart, J. W. Paulley, J. S. Rivers and E. K. Westlake.—p. 226.

Lancet, London

2:845-894 (Nov. 10) 1951

Vascular Spasm. G. W. Pickering.—p. 845.
Fluid Balance in Congestive Cardiac Failure: Two Mechanisms in Diuresis. T. E. Lowe.—p. 851.
*Chronic Mercury Poisoning in Men Repairing Direct-Current Meters. P. L. Bidstrup, J. A. Bonnell, D. G. Harvey and S. Locket.—p. 856.
Pantothenic Acid in Paralytic Ileus. J. E. Jacques.—p. 861.
Successful Transfusion of Previously Frozen Human Red Cells. P. L. Mollison and H. A. Sloviter.—p. 862.
Pulmonary Embolism After Treatment with Heparin. R. M. Cadenhead.—p. 865.
Potentiation of Antibacterial Activity of Sulphathiazole by Glutamine. G. C. Ware.—p. 865.

Mercury Poisoning in Men Repairing Direct-Current Meters.—Five men who were employed in workshops where direct-current (D. C.) electric meters were repaired were found to have chronic mercury poisoning. To determine the incidence of chronic mercury poisoning in this industry, men employed as meter repairers in the London area were examined. Arrangements were made for clinical examination of the exposed men, estimation of mercury excreted in the urine in 24 hours, and estimation of mercury present in the atmosphere in each workshop. Of the 161 men examined, 103 repaired D. C. meters and 58 tested these meters or repaired alternating-current (A. C.) meters. Although there is no direct contact with mercury in the latter work, it is sometimes done in the same workshop where D. C. meters are repaired, and the men are therefore exposed to mercury in the atmosphere. Symptoms or signs of chronic mercury poisoning were found in 27 men, all of whom repaired D. C. meters. No case of chronic mercury poisoning was detected among 58 men who tested meters or repaired A. C. meters. In doubtful cases the diagnosis was confirmed by estimating the amount of mercury excreted in the urine. The excretion of more than 300 γ of mercury in 24 hours was usually accompanied by symptoms of chronic mercury poisoning, which in some cases had been attributed to neurosis. The concentration of mercury in the working atmosphere was much higher during the winter months, except where exhaust ventilation had been installed. The incidence of mercury poisoning varied according to the concentration of mercury in the working atmosphere. Measures to prevent mercury poisoning are suggested.

2:895-946 (Nov. 17) 1951

The Arts of Medicine and Their Future. F. M. R. Walshe.—p. 895.
*Treatment of Hypertension with Hexamethonium Bromide. E. A. Murphy.—p. 899.
Action of Dehydro-Ascorbic Acid and Alloxan on Tuberculin-Sensitivity in Guineapigs. D. A. Long, A. A. Miles and W. L. M. Perry.—p. 902.
*Toxoplasma Infection in English Children: Survey with Toxoplasmin Intradermal Antigen. O. D. Fisher.—p. 904.
Microchromatographic Method for Separation of Certain Fractions of 17-Ketosteroids in Human Urine. M. H. Pond.—p. 906.
Chronic Osteomyelitis Treated by Primary Closure with Antibiotic Control. A. K. Basu.—p. 909.
Typhoid Osteomyelitis Treated by Surgery and Chloromycetin. J. D. Morgan.—p. 911.
Low Plasma-Potassium Levels in Acute Leukaemia. A. Videbaek.—p. 912.
Antiglobulin (Coombs) Test in Brucellosis. M. M. Wilson and E. V. O. Merrifield.—p. 913.
Recovery of Newborn Child from Bact. Coli Meningitis. J. S. Ebsworth and D. G. Leys.—p. 914.

Hexamethonium Bromide in Hypertension.—Murphy used hexamethonium bromide in treatment of 43 patients who had various degrees of hypertension. The drug was given orally or subcutaneously, but whenever possible the oral route was used for ease of administration. When the drug was unsuccessful orally, it was given parenterally. Some of the patients had previously been treated without success by sympathectomy or with potassium thiocyanate. Results obtained with hexamethonium bromide were encouraging. The most dramatic emprovements were seen in patients with severe retinopathy and placid temperament. The nature and properties of the hypertension must be determined before treatment is decided on. Possible side-effects are mentioned and measures to counteract them are outlined. It has been suggested that long-term improvement is due solely to the bromide ion, but reasons are given why this explanation is not acceptable. Satisfactory preliminary results obtained with hexamethonium bitartrate are mentioned.

Toxoplasmosis in English Children.—Toxoplasmosis is now recognized as a disease of world-wide distribution. In the commonly recorded form the infection is congenital and may be characterized by hydrocephalus, cerebral calcification, and choroidoretinitis. The acquired infection has been recognized in several clinical forms; in children it occurs as a nonsuppurative meningoencephalitis, and in adults as an enteric or rickettsial type of illness. However, the infection may be revealed only by the presence of toxoplasma antibodies in the serum. To determine the incidence of toxoplasma infection in English children, their sensitivity to intradermal inoculations of toxoplasmin was used like the tuberculin reaction in tuberculosis. The preparation of the toxoplasmin antigen and results of intradermal inoculation are described. A large-scale survey of children by this method was correlated with serological investigation of toxoplasma antibodies by the dye test and the complement-fixation test. The incidence of infection was found to be insignificant in the earliest age group (up to 4 years), rising to 7% in the third age group (10 to 14 years), and to 17.5% in the adult group (15 years or more). It is concluded that toxoplasmin reaction is a reliable means of detecting toxoplasma infection in population surveys and as a screening test for suspected cases.

Medical Journal of Australia, Sydney

2:485-516 (Oct. 13) 1951

Influence of Intrathecally Administered Adrenaline on Adrenal Cortex. S. Rose.—p. 485.
Perineal Dissection in Excision of Carcinoma of Rectum. E. S. R. Hughes.—p. 499.
Use of Skin Grafting in Hernial Repair. J. C. B. Allen.—p. 502.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:3017-3080 (Oct. 13) 1951. **Partial Index**

*Dupuytren's Contracture and Epilepsy. W. Kramer and J. Luten.—p. 3023.
Acanthosis Nigricans. A. R. F. Somers.—p. 3029.
A Case of Infectious Mononucleosis Transmitted by Blood Transfusion. J. F. deVos and F. H. Kuipers.—p. 3036.

Dupuytren's Contracture and Epilepsy.—Kramer and Luten examined 554 epileptic patients for the presence of Dupuytren's contracture and detected this form of fibrosis in 38 or 7%. This incidence is not as high as that reported by other investigators (40% and 52%), but over half of the epileptics studied were less than 20 years old. Among 50 epileptics between 40 and 50 years of age there were 11 (or 22%) with Dupuytren's contracture and among 31 between 50 and 60 there were 9 (29%). The authors had previously observed that Dupuytren's contracture is often associated with other connective tissue lesions. Since Scandinavian authors had stated that such associated lesions were particularly frequent in epileptics, the authors list the incidence of Dupuytren's contracture and knuckle pads, plantar fibroma, and humeroscapular periarthrosis, which were relatively frequent. The authors feel that the increased incidence of Dupuytren's contracture in epileptics is related to the prolonged use of large doses of barbiturates rather than to the epilepsy. In some cases trauma may be a factor. The authors gained the impression that epileptics with Dupuytren's contracture are of a constitutional type, with signs of status dysraphicus. It is assumed that this constitutional anomaly favors the development of Dupuytren's contracture.

Nordisk Medicin, Stockholm

46:1437-1476 (Sept. 26) 1951. **Partial Index**

Fractures of Malar Bone. T. Skoog.—p. 1440.
*Curare in Abdominal Surgery. A. Lidström and S. O. Liljedahl.—p. 1445.
Result of Osteosynthesis with Modified Nail in Fractures of Mid-Neck of Femur. A. Ekengren.—p. 1449.
Acute Atrophy of Bones of Shoulder Joint: Osteoarthropathy in Syringomyelia. M. Hauge.—p. 1450.

Curare in Abdominal Surgery.—On the basis of their use of curare in conjunction with "narkotal" (an intravenous barbiturate) and nitrous oxide or ether in 692 abdominal operations, Lidström and Liljedahl conclude that curare is a valuable adjunct to anesthesia in all intra-abdominal surgery. The frequency of complications during and after operation is low. The use of curare at the beginning of ether anesthesia offers several advantages. Curare during ether anesthesia should be administered in small doses (1.5 to 3 mg.). Administration of curare in the final stage of anesthesia is cautioned against, as it apparently increases the risk of postoperative complications. Curare anesthesia should always be administered by personnel fully experienced in anesthesia and familiar with endotracheal intubation.

Practitioner, London

167:305-470 (Oct.) 1951. **Partial Index**

The Changing Face of Medicine 1868-1951. H. Dale.—p. 309.
Social Background of Medicine. H. Bashford.—p. 315.
Trends of General Practice: Hundred Years in Yorkshire Dale. W. N Pickles.—p. 322.
Advances in Medicine. H. Cohen.—p. 330.
Advances in Surgery. D. C. Balfour.—p. 343.

167:471-572 (Nov.) 1951. **Partial Index**

Treatment of Acute Otitis Media. J. P. Monkhouse.—p. 475.
Infections of Outer Ear. E. G. Collins.—p. 481.
Problems of Chronic Running Ear. A. B. Thomas.—p. 491.
Treatment of Otosclerosis. T. Cawthorne.—p. 499.
Use and Limitation of Hearing Aids. F. C. Ormerod.—p. 504.
Sociological Aspects of Deafness. R. S. Stevenson.—p. 510.
Principles of General Anaesthesia in Childhood. P. Westhead.—p. 514.
Medical Problems of the Aged Sick: Practical Approach to Bed Sores, Incontinence and Restlessness. T. N. Rudd.—p. 521.

Presse Médicale, Paris

59:1381-1412 (Oct. 24) 1951. **Partial Index**

Possible Presence of a Demyelinating Process Affecting the Spinal Cord in Acute Anterior Poliomyelitis, and Its Occasional Significance. P. Mollaret, I. Bertrand and H. Mollaret.—p. 1381.
*Combined Use of Chaulmoogra Oil and Streptomycin in Treatment of Pulmonary Tuberculosis. H. Warembourg and G. Niquet.—p. 1387.
*Treatment of Dupuytren's Contracture by Plastic Surgery Using Z-Shaped Incisions Along the Length of the Finger up to the Center of the Palm. M. Iselin and G. D. Dieckmann.—p. 1394.

Chaulmoogra Oil in Pulmonary Tuberculosis.—Combined treatment with chaulmoogra oil and streptomycin or *p*-aminosalicylic acid was given to 20 patients with advanced pulmonary tuberculosis. Administration of chaulmoogra oil was instituted when streptomycin and/or *p*-aminosalicylic acid had been used previously and seemed no longer effective clinically and roentgenologically. Injections of 2 cc. of chaulmoogra oil (the entire product, not just some of its constituents), with 800 units per gram of vitamin A added, were given daily for seven days, and then 5 cc. of the oil were administered daily for 23 days. Of the 20 patients, 14 obtained good results with persistent improvement of the pulmonary lesions revealed by roentgenologic examination and improvement of the general condition, with increased appetite and gain in weight; 2 patients were improved temporarily and 4 were therapeutic failures. In two patients with good results from two months' treatment with chaulmoogra oil, the former resistance of the Koch bacillus (obtained from the patient's sputum) to 50 units of streptomycin in vitro decreased to a sensitivity to 1 unit of streptomycin in vitro. The chaulmoogra oil was well tolerated, with no untoward reactions. Chaulmoogra oil therefore deserves a place in the therapeutic armamentarium of pulmonary tuberculosis.

Plastic Surgery in Dupuytren's Contracture.—A new method of plastic surgery was practiced in 40 patients with Dupuytren's contracture. Z-shaped incisions were extended in a longitudinal line over the entire length of the involved finger up to the center of the palm. The palmar aponeurosis was completely extirpated through these incisions and the finger then was straightened. Each of the small triangular skin flaps resulting from the z-shaped incisions was transposed with the flap opposite it to relax the tension, and the flaps were held in place with steel wire sutures. These were not removed for at least two weeks, and the hand was placed on a well padded dorsal splint with the fingers slightly flexed. The wounds healed in an average time of 31 days. Good results with complete extension and flexion of fingers were obtained in 24 patients, moderate results with limited extension or limited flexion in 8 patients, and unsatisfactory results in 7, with amputation of the finger required in 5 and recurrence in 2. One patient was not followed. A classification of Dupuytren's contracture in four degrees has been

attempted. The greatest percentage of therapeutic failures or of unsatisfactory results were observed among the patients with involvement of the fifth finger, who also had the highest incidence of fourth degree lesions. Patients with involvement of two or more fingers presented the most difficult technical problems. The results obtained in the authors' cases proved that two-thirds of the patients may obtain recovery with surgical treatment and only from this, while failures in about 15% must be expected.

59:1433-1452 (Nov. 3) 1951

Esterized Fatty Acids in Pathology of Liver. E. Chabrol, M. Böszörményi, P. Fallot and P. Deslypère.—p. 1433.
*Behavior of Heart of Patients with Endocarditis Treated with Antibiotics. P. Broustet.—p. 1434.

Antibiotics in Endocarditis.—Of 23 patients with acute bacterial endocarditis treated with penicillin, 15 had functional disturbances of the cardiac muscle during the febrile stage of the disease or immediately after the temperature returned to normal. Although cardiac decompensation occurs rarely in endocarditis, cardiac dilatation and asystoles may result from valvular destruction or involvement of the myocardium. According to the classic concept, the antibiotics do not exert a favorable influence on cases of endocarditis complicated by cardiac failure; certain investigators even consider this complication irreversible. But there are exceptions. In four of the author's patients, following administration of penicillin, the asystoles disappeared simultaneously with the restoration of the temperature to normal. The functional symptoms subsided as the infection cleared, even in two patients who were not given cardiac tonics. In contrast to these observations, the antibiotics, particularly penicillin, may cause sudden cardiac failure associated with coronary occlusion in patients with endocarditis. It is suggested that these undesirable side-effects may be the result of the allergenic power of certain antibiotics. Thus the response of the heart to the antibiotics varies and each patient presents an individual problem. Therapeutic results may be improved by determining the infectious etiology of the asystoles, early institution of treatment, and use of the antibiotic indicated for the pathogenic agent.

59:1493-1512 (Nov. 14) 1951. **Partial Index**

*Treatment of Bouillaud's Disease with Cortisone and Corticotropin. F. Coste and M. Oury.—p. 1493.
Part Played by Reflux in Digestive Pathology, Particularly in Pathogenesis of Esophageal Dyskinesia, Esophagitis, Dyspepsia and Gastritis. A. Lambling.—p. 1496.

Cortisone and Corticotropin in Rheumatic Heart Disease.—Of 43 patients with rheumatic heart disease treated with cortisone and corticotropin (ACTH), 25 presented symptoms of severe rheumatic carditis. Of these 25, 4 died from malignant rheumatic heart disease, but only 2 who died had been treated with the hormones for more than three days. Two patients were therapeutic failures, while 19 were improved considerably. Of the remaining 18 patients, 5 had recurrent carditis with rheumatic symptoms that subsided rapidly while the signs of chronic cardiovalvulitis remained unchanged; of 4 patients with recent carditis, 3 made a complete recovery; the hearts of 9 patients with acute articular rheumatism, 5 of whom apparently had endocarditis, appeared normal on clinical, roentgenologic, and electrocardiographic examination at the termination of treatment. Because of the small number of patients with rheumatic heart disease treated with cortisone and corticotropin, definite instructions for treatment cannot be given, but the authors' experience suggests that to check the inflammatory process as rapidly as possible treatment should be started with corticotropin, while later on either corticotropin or cortisone may be employed. At least four daily injections of corticotropin at regular intervals are advisable, while injections of cortisone in microcrystalline suspension may be given every second day. In cases of acute articular rheumatism without carditis or with incipient carditis, treatment should be given for four weeks, while in cases of severe rheumatic heart disease it should be continued for more than two months. The results obtained by the authors suggest that it is possible to control some of the manifestations of rheumatic heart disease with corticotropin or cortisone. The general and functional rheumatic symptoms responded promptly, but, contrary to Hench, the French workers observed that tachycardia requires two to three weeks to disappear, and they did not observe secondary bradycardia. Erythrocyte sedimentation rates and fibremia responded more slowly than rheumatic symptoms. Pericarditis showed pronounced improvement, as did endocarditis and myocarditis. Although the hormone treatment might not shorten the acute phase of rheumatic heart disease, it seems to control progressive involvement, particularly of the tissues of the heart. Satisfactory results depend on early treatment; cardiac sequelae may be prevented by starting treatment before the occurrence of cardiac involvement or in its initial stage. Oral administration of penicillin seems to aid in the prevention of relapses.

Riv. di Pat. e Clin. della Tuberc., Bologna

24:195-256 (July-Aug.) 1951

Extrapleural Pneumothorax Substituting Inefficient Intrapleural Pneumothorax. G. Zorzoli and A. Valli.—p. 195.
*Simultaneous Bilateral Pneumothorax: Considerations on 340 Cases. N. Sanguigno and A. Vazzana.—p. 200.
Pulmonary Tuberculosis and Congenital Cardiopathy in Unusual Case of Cyanosis. G. Izzo.—p. 215.
*Progressive Tuberculous Polyneuritic Muscular Atrophy. G. Faenzi and A. Mulargia.—p. 238.

Simultaneous Bilateral Pneumothorax.—Simultaneous bilateral pneumothorax was induced in 340 hospitalized patients with pulmonary tuberculosis and was continued for two and one-half years. The second pneumothorax was instituted one to several weeks after the first. The quantity of gas introduced, intrapleural pressure, and frequency of refills depended on the patient's resistance and tolerance. Patients over 50 and those with associated intestinal tuberculosis and heart or kidney disturbances were excluded. Pleurisy, empyema, perforation of the lung, and appearance of new tuberculous foci were the commonest complications. A follow-up five or more years later showed that 94 patients (27.7%) were cured. Pleurisy had occurred in 42 of these patients, and perforation of the lung in 2. Intrapleural pneumolysis or phrenic avulsion had been performed in 15. The condition was stationary in 23 patients, and 27 were not followed. Death occurred in 196 (57.6%). Before pneumothorax the condition of 30 of these patients was critical. In 30 a transient improvement due to the treatment was so great that they were able to resume their work temporarily. Death was due to pleurisy in 84 patients, to perforation of the lung in 15, to hemorrhage in 21, to meningitis in 4, and to toxemia and cardiorespiratory insufficiency in others. The mortality appears high, but there is reason to believe that if simultaneous bilateral pneumothorax had not been performed, the patients would have died sooner and the mortality would have been higher. The treatment was carried out before antibiotic therapy was introduced. With antibiotic drugs to combat complications this treatment may yield better results.

Progressive Tuberculous Polyneuritic Muscular Atrophy.—Pneumothorax was induced in a man, 45, who had pulmonary tuberculosis. Several months later in November, 1949, pain developed in the joints, with high temperature and chills. A year later these symptoms were aggravated by formication, prickling, and sense of cold, first in the lower and then in the upper extremities. Hypotonia was pronounced, and the patient's general condition was poor. Atrophy was observed in the legs and subsequently extended to the thighs, forearms, arms, and later to the feet and hands. Pain and paresthesia increased when the patient was standing. Sudden attacks of muscular hyperesthesia and hyperalgia and marked muscular atrophy in the distal parts of the extremities were the main characteristics of this case. The mode of onset and quick progression of atrophy, the diminution of deep reflexes, the absence of fibrotendinous reflexes, and sensory disturbances justified a diagnosis of tuberculous polyneuritic muscular atrophy caused by tuberculous toxins. This disease entity progresses to death because the toxic stimulus is continuous and causes irreversible degenerative alterations. Antibiotic drugs and massive doses of thiamine (vitamin B_1) were administered to this patient for a long time. His condition was not influenced and is now extremely poor.

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Schweizerische medizinische Wochenschrift, Basel

81:1097-1116 (Nov. 10) 1951. **Partial Index**

*Significance of Prolonged Administration of Thiouracil with Respect to Proliferation of Thyroid Tissue. E. Herrmann.—p. 1097.
Correlation Between Plasma Proteins and Tissue. C. Wunderly and F. Wuhrmann.—p. 1102.
Effect of Total Heart Extract on Perfusion of Coronary Vessels of Heart by Blood. H. Blömer and G. Schimert.—p. 1108.

Thyroid Proliferation After Prolonged Thiouracil Therapy.—Two patients, a woman aged 54 and a man aged 69, with toxic diffuse goiter were treated with methyl thiouracil for 3 years and 3 years and 10 months, respectively. The total doses of the drug administered were 21.25 gm. and 139.63 gm. Thyroidectomy was performed on both patients. In both microscopic examination of the specimen revealed toxic diffuse parenchymatous hyperplasia with numerous microfollicular and trabecular adenoma anlages. Adenomas with degeneration into a proliferating struma in the woman and into solid, adenopapillomatous carcinoma in the man were found. In addition a hemangioendothelioma was observed in the latter patient. Rupture of numerous vessels, perforation of the capsule, and infiltrative growth were present in both instances. Animal experiments performed by American and British investigators showed that the time factor plays a considerable part in the production of adenomas and malignant tumors observed in rats that had been treated with thiouracil or its derivatives for 6 to 20 months. The author agrees with the concept of these investigators that the occurrence of adenoma and occasionally of carcinoma, though not caused directly by thiouracil, may be the effect of increased secretion of thyrotropic hormone due to deficient formation of thyroxin, or may possibly be the effect of iodine deficiency. Thiouracil and its derivatives should not be considered carcinogenic, but capable of producing thyroid adenomas with possible secondary malignant degeneration. The author therefore cautions against too long continued administration of thiouracil. He advocates surgical treatment of patients with recurrence after a remission had been obtained with thiouracil or its derivatives.

Semaine des Hôpitaux de Paris

27:3333-3370 (Nov. 14) 1951

*Treatment of Hypertension by Interrupted Prolonged Sleep. G. B. Feldman.—p. 3333.
Steroid Hormones and Inflammatory Reaction. A. Lichtwitz, S. de Sèze, G. Thiéry and others.—p. 3337.
Viruses of Seasonal Encephalitis and Their Tropical Origin. P. Lépine.—p. 3354.

Treatment of Hypertension by Prolonged Sleep.—On the basis of Pavlov's concept of the internal inhibition of conditioned reflexes by sleep, the author treated 46 patients with neurogenic hypertension by interrupted prolonged sleep. The 39 women and 7 men between 21 and 55 who were studied were hospitalized for about 30 days. For the first 10 days the patients rested in bed and were subjected to various examinations including oscillometry, measuring of venous pressure and circulatory velocity, capillaroscopy, electrocardiograms, and examination of the fundus of the eyes. Ophthalmodynamometric measurements and photographs of the fundus of the eyes were taken in 11 patients. Laboratory examinations included determinations of blood cholesterol, nonprotein nitrogen, alkali reserve, exploration of the glycopexic function of the liver, function of the kidneys, and basal metabolic rate. On the 11th day treatment by sleep was instituted. Sleep was induced by the administration of amobarbital sodium, which was preferred to phenobarbital because it is readily eliminated. The doses used for the treatment of the first five patients proved to be too high; the doses employed in the remaining 41 patients were 0.3 gm. given twice daily by rectal route or 0.2 gm. given orally in the morning and in the evening for 10 days. The total dose of the drug varied from 4.5 gm. to 6.5 gm. On the fourth or fifth day of the treatment, when the narcotic effect of the drug was diminishing, 0.25 gm. of aminopyrine was given twice a day. The synergistic effect of the two drugs was observed frequently. Following the administration of the drug in the morning the patients slept for three and a half to four hours. While still somnolent they were given a tablespoonful of Bechterew's mixture, and after that they slept again for three and a half to four hours. They then ate their dinner, received the second dose of the drug, and slept through the entire night. Thus an average of 18 hours sleep was obtained in the course of 24 hours. Complications in the central nervous system or other organs did not occur. Satisfactory results with drop of the arterial pressure, disappearance of irritability and anxiety, and restoration of full working capacity were obtained in 28 patients. Fairly good results were obtained in additional 9 patients, while the remaining 9 were therapeutic failures.

South African Medical Journal, Cape Town

25:773-788 (Oct. 27) 1951. **Partial Index**

*Fat Necrosis of Breast. I. Opeskin.—p. 778.
Sickle Cell Anaemia: Report of Case with Note on Therapy. I. J. Grek and M. Findlay.—p. 780.
Late Successful Arterial Embolectomy. H. Katz.—p. 784.

Fat Necrosis of Breast.—Fat necrosis of the breast may resemble the clinical signs of carcinoma very closely, as indicated in 45 cases, in 12 of which a radical mastectomy was performed. Even in early fat necrosis there may be central liquefaction with production of yellowish, oily fluid. Very soon the area appears chalky and is invaded by fibrous tissue that splits it up into rounded and irregular fragments. The lesion feels firm, but it never has the hardness of scirrhous carcinoma. Sometimes the lesion is slightly pigmented by hemosiderin. The tumor may be differentiated from carcinoma by absence of the characteristic yellow spots of epithelial debris and infiltration in surrounding tissues, although there is some adherence. After discussing the microscopic appearance of the lesion, the author describes the history of a patient in whom fat necrosis of the breast was at first diagnosed as inoperable scirrhous carcinoma, but the following factors suggested the advisability of a biopsy before treatment: the history of such a large hard mass was short; the affected nipple was lower than normal and not retracted; the pigmented area around the areola was not typical of carcinoma; and the axillary glands were small and not hard. The author stresses that rapid increase in the size of a hard mass in a breast should suggest the possibility of fat necrosis, especially when associated with a history of trauma. The macroscopic appearance of fat necrosis is typical and in doubtful cases the mass should be incised before radical mastectomy is done.

Ugeskrift for Laeger, Copenhagen

113:1397-1426 (Oct. 18) 1951. **Partial Index**

*Fetal Toxoplasmosis. V. A. Jensen.—p. 1397.
Problems in Verification of Foot-and-Mouth Disease in Man. E. Michelsen.—p. 1401.
Streptomycin Treatment of Acute Tuberculous Otitis Media. P. M. Christensen.—p. 1406.
After Administration of Dihydrostreptomycin: Case. J. Guldberg-Møller.—p. 1409.
Kveim's Reaction Applied in Diagnosis of Benign Lymphogranulomatosis (Schaumann). G. Søndergaard.—p. 1412.

Fetal Toxoplasmosis.—Jensen says that toxoplasmosis in adults is usually latent and is manifested by development of specific antibodies in the blood or by the fact that children with manifest toxoplasmosis are born to infected mothers. The cardinal symptoms in congenital toxoplasmosis are bilateral chorioretinitis, internal hydrocephalus, intracerebral calcifications, and convulsions. Toxoplasma are transmitted from mother to child in the uterus. Three infants with hydrocephalus and one infant with dyssynostosis cranii, all found to have toxoplasmosis, were admitted in the neurosurgical department of Aarhus Kommunehospital during the last two years. The results of histological examination of the retina in the three fatal cases are described in detail. One infant was a twin; his twin sister is well and has a normal fundus. One of the mothers later gave birth to a healthy child. Tissues in the differentiation stage are more susceptible to intrauterine injury by virus than other tissues, which is the reason that the retina and chorioidea in the macula region, where differentiation of tissue occurs late, are oftenest the place of least resistance to toxoplasma.

BOOK REVIEWS

The Electrical Activity of the Nervous System: A Textbook for Students. By Mary A. B. Brazier, B.Sc., Ph.D. Cloth. $5. Pp. 220, with 96 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

This book summarizes for students of neurophysiology the facts thus far gathered relating to the electrical excitation of nerves, the nature of the nerve impulse, and the electrical phenomena observed in nerve fibers and in masses of nervous tissue. It is not intended to be a technical manual and presupposes a considerable knowledge of anatomy, as well as experience in the laboratory, on the part of the student. Nevertheless, the author's fortunate style lends a certain vividness to the presentation. This will be appreciated by those who recall the oppressive dullness of some comparable works written in the past. The wealth of new information presented is gratifying, and the reader cannot help imagining the pleasure that Galvani, Helmholtz, and Du Bois-Reymond would take in the recent developments in their field of research. Special praise is merited by the concluding chapters on the electrical activity of the eye, ear, other sense organs, and the brain, with the judicious treatment of the subject of normal and abnormal electroencephalograms. It is unlikely that every student will understand the allusion to the automatic electronic analyzer (page 198) or be aware of the pitfalls of harmonic analysis, but an excellent bibliography at the end of each chapter gives clues to unanswered questions. There is also a commendable index. This book should be available in every library devoted to the basic medical sciences.

Bacterial Toxins. By W. E. van Heyningen, M.A., M.Sc., Ph.D., Senior Research Officer, Sir William Dunn School of Pathology, University of Oxford. Cloth. $3.50. Pp. 133, with 12 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford; Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This monograph was written because the subject of bacterial toxins has been neglected in most textbooks. Discussions of toxins of the gram-positive bacteria occupy most of the text; these include toxins of the clostridia, the corynebacteria, the streptococci, and the staphylococci. The toxins of these organisms are generally more toxic than those of the gram-negative group, and they are capable of being neutralized and toxoids can be formed from them. The gram-negative group includes Shigella dysenteriae, Brucella, melitensis, Vibrio cholerae, the neisseriace, hemophilus pertussis, Pasteurella pestis, the Rickettsia, and the viruses. Most of these are endotoxins about which less is known. References to more than 400 published articles are given. The book is recommended to anyone interested in this subject.

Amenorrhea. By Lawrence M. Randall, M.D., and Thomas W. McElin, M.D. Publication number 109, American Lecture Series, monograph in American Lectures in Endocrinology. Edited by Willard O. Thompson, M.D., Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago. Cloth. $2.25. Pp. 74. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This is a short monograph on the classification, investigation, and treatment of amenorrhea of primary and secondary origin. Unfortunately, some confusion is caused by the citation of many authorities without an attempt to organize or draw conclusions from their material. However, this criticism, if it can be called that, does not extend to the excellent review of the Russian investigations and the section on therapy. In the latter, the roles of the estrogens, thyroid, gonadotropins, progesterone, and combined hormonal therapy are briefly reviewed by abstracts of the literature. Less frequently utilized forms of therapy, such as roentgen ray techniques and neostigmine, are also included.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

A Textbook of General Physiology. By Hugh Davson, D.Sc., Scientific Staff, Medical Research Council, London. Cloth. $7. Pp. 659, with 288 illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, [1951].

The author has collected in this book the results of modern research of the general physiologist, who "attempts to explain living phenomena in terms of concepts familiar in the basic sciences of physics and chemistry." The book has six major divisions: the structural basis of living matter, the transformations of energy in living systems, the transport of water and solutes, the characteristics of excitable tissue, the mechanism of muscle contraction, and the emission and effects of light. The intention of the author was to produce a work comparable to the classic "Principles of General Physiology" of William Bayliss. In this he has largely succeeded, for he has caught the spirit of his predecessor admirably. Though Bayliss may never have heard of semantics and operational analysis, he had the good sense to avoid defining a given word in terms of other indefinable words; he illustrated general principles by means of specific instances, and he recognized the need of describing apparatus and procedure before stating results and conclusions. These features also characterize the present volume, and the present author has had the advantage that many of the things that could be pictured only mentally by Bayliss can now be seen and measured by such methods as roentgen ray diffraction, electron microscopy, phase microscopy, ultrafiltration, ultracentrifugation, electrophoresis, and the use of radioactive isotopes. Furthermore, the imitation of living systems by arrangements of cells and condensers has undergone unexpected development.

The author expresses his regret at the omission of a number of subjects; to his list might be added the production, effects, and perception of sonic and ultrasonic vibrations. It is to be hoped that such material will be supplied in a future edition. The present edition deserves high praise for clarity of text, beauty of illustrations, helpful bibliographies, and good index.

Experimental Physiology for Medical Students. By D. T. Harris, M.D., D.Sc., F.Inst.P., H. P. Gilding, M.A., M.D., Professor of Physiology, University, Birmingham, and W. A. M. Smart, B.Sc., M.B., B.S. Fifth edition. Cloth. 21s. Pp. 305, with 267 illustrations. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London W.1, 1951.

The first section of this excellent book is devoted to experiments in physiology and the second to experiments in pharmacology. Both sections afford illustrations of the handicaps under which these two subjects must be taught in England because of the lingering influence of antivivisectionists. It is gratifying, however, to find the metric system used throughout; in other respects, too, the book is abreast of the times.

Commendable are the figures, which include a sufficient number of wiring diagrams to stimulate the student's interest in audiometers and similar appurtenances of modern physical medicine. The section on special senses contains many good experiments. The experiments on taste (page 266) could be enriched by the inclusion of phenylthiourea, which not only impresses the student with the importance of individual differences but is of historic interest because of the developments that have followed its discovery. The subject of basal metabolic rate could be freed of a source of much confusion and error by eliminating the surface area concept, following the recommendations of Dreyer. In connection with sphygmomanometry (page 101) it might be well to reproduce the carefully prepared recommendations of the Committee of the American Heart Association to Revise Standardization of Blood Pressure Readings. The various methods of sphygmomanometry are also an excellent source of data for the calculation of reliability indexes and for other exercises in practical biometry. At this and several other points in the book the authors might well introduce some of the simpler concepts of statistical methodology, particularly that of the contratest or "control" and the fourfold table. In the pharma-

cology section it must be noted that the statement "Bronchoconstrictors . . . are only of pharmacological interest" (page 289) is no longer true, since the development of "nerve gases" as a threat in warfare and of organic insecticides in agriculture, and that Tyrode's solution (pages 276 and 299) ought to be replaced by stabler media, such as the Sollmann-Rademaekers solution.

The book is attractive in appearance, the printing is remarkably free from errors, and there is a good index. It is to be recommended to physiologists as a rich source of inspiration and practical suggestions.

Biological Effects of External Beta Radiation. Edited by Raymond E. Zirkle, Professor of Radiobiology, Institute of Radiobiology and Biophysics, University of Chicago, Chicago. National Nuclear Energy Series: Manhattan Project Technical Section. Division IV: Plutonium Project Record, Volume 22 E. Cloth. $3.25. Pp. 242, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1951.

This volume records some of the results of research done under the Manhattan Project and the Atomic Energy Commission between 1942 and 1945. It has eight contributing authors and 16 chapters. The greater part of the results reported were obtained by Dr. I. R. Raper while at the Clinton Laboratories during World War II.

The chapters entitled "Techniques of External Irradiation with Beta Rays" records the methods used by the group at the Clinton Laboratories for preparing and evaluating the radioactive sources. Although some work under the Manhattan Project was done with radioactive strontium (Sr^{89}) and radioactive yttrium (Y^{91}), the lack of suitable intense sources of these isotopes prevented their use in the biological experiments; consequently, these experiments were limited to the use of radioactive phosphorus (P^{32}). The balance of the book records the effects on various laboratory animals of beta irradiation as compared with gamma irradiation, showing gross and microscopic effects of restricted and total surface irradiation, additive effects, delayed effects, and recovery rates, blood changes and metabolic derangements. The tumor inducing action of superficial radiation is discussed in a separate chapter. The rapidly increasing application of artificial radioactive isotopes to medical problems makes this volume of great value to those already using these agents or to those contemplating their use.

Journey Together. By Turnley Walker. Cloth. $2.50. Pp. 144. David McKay Company, Inc., 225 Park Ave., New York 17, 1951.

This is a fascinating and well-written autobiography telling the story of one man's rehabilitation after he was handicapped by the residual paralysis of poliomyelitis. The reader's interest will gather momentum as he follows the story of the author's finding himself as a person again and his return to the world outside the protective security of the hospital. This book provides a glimpse of the universal despair, as well as the gratifying feeling that follows mastery over handicap, felt by all those acutely stricken with a disabling disease. It could well be used as a source of encouragement by many of the handicapped in bringing about a psychological adjustment to their disability, and could provide them with determination to develop their remaining faculties to a point where they can again lead happy and useful lives.

Caring for the Premature Baby. By Lillian Saltzman. Cloth. $2.50. Pp. 142, with illustrations. Chapman & Grimes, Publishers, 30 Winchester St., Boston 16, 1951.

This is an excellent book, directed to the layman, concerning the minute technicalities of care of the premature infant. It should prove helpful to those in communities in which home births are prevalent and hospital care for premature infants is not available, and should be of value to both practical and trained nurses. The book covers general facts concerning the anatomy and physiology of the premature infant and its early care and gives specific details concerning infection, cyanosis, clothing, bathing, and feeding. The problem of humidity does not receive sufficient stress; it is now generally recognized that adequate humidity is essential for the premature infant. Also, the oxygen concentration recommended by the author for these infants seems too high. Informative discussions of the various types of incubators and of diarrhea and intestinal disorders are included. Persons entrusted with the care of a premature infant should find this book of assistance.

Leibesübungen mit Körperbeschädigten: Ein Lehr- und Arbeitsbuch für Körperbehinderte und ihre Betreuer. Von Hans Lorenzen. Neue Folge Heft 45, Arbeit und Gesundheit; Sozialmedizinische Schriftenreihe aus dem Gebiete des Bundesministeriums für Arbeit. Herausgegeben von Professor Dr. phil. et med. M. Bauer und Dr. med. F. Paetzold. Paper. 7.50 marks. Pp. 218, with 182 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This is an interesting monograph on the subject of exercises for persons with bodily handicaps. Coming out of Germany, the traditional bulwark of formalism in physical education and in sports, this book shows a remarkable advance in the concept of making physical education a source of pleasure in the actual doing, as well as a means toward an objective, such as body building, and, in the case of the handicapped, rehabilitation. The book deals with organizations and methods, with general body development, with the medicine ball and the usefulness of tumbling, swimming, diving, and lifesaving, and with many variations of competitive sports for arm and leg amputees and others with various forms of body deformities. It is concerned particularly with war casualties but is equally applicable to those handicapped from any other cause. Allowing for the fact that, despite its progress toward informality, it still contains considerable evidence of characteristic German formalism, this book contains valuable suggestions for physicians or physical educators dealing with exercise for the handicapped. The illustrations are numerous and clear, and they help to overcome language difficulties for those who do not read German fluently.

Comparative Physiology of the Thyroid and Parathyroid Glands. By Walter Fleischmann, M.D., Ph.D., Instructor in Pediatrics, Johns Hopkins University School of Medicine, Baltimore. Publication number 118, American Lecture Series, monograph in American Lectures in Endocrinology. Edited by Willard O. Thompson, M.D., Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago. Cloth. $2.25. Pp. 78. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This monograph contains a review of literature dealing with the comparative physiology of the thyroid and parathyroid glands. The author, who has himself contributed widely to this field, has covered the subject adequately, describing pertinent discoveries in organisms ranging from ammocoetes to man. The hormones subserve such basic functions in the animal economy that it is not surprising to learn they are identical throughout the vertebrate phylum. A study of comparative endocrinology is thus not without value in understanding hormonal functions in the human. The author has included a bibliography of over 100 references. Although the monograph is of value primarily to the experimental endocrinologist, the internist will find it of some interest. The format and style are good; a more extensive treatment of the subject and inclusion of illustrations would have been desirable.

The Curriculum in Health and Physical Education. By Leslie W. Irwin, Ph.D., Professor of Health and Physical Education, School of Education, Boston University, Boston. Second edition. Cloth. $4. Pp. 382. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This book covers the curriculum in physical education in some detail and school health and safety in a more general way. A discussion of the place of physical education in modern living and education is followed by a rather specific outline of activities for the various grade levels. Descriptions of intramural, interschool, and informal sports programs suitable for the various age groups are also presented, with emphasis placed on the need for the type of organization and administration that will permit desirable health and educational outcomes. A strong plea is made for careful consideration of individual differences among pupils in the planning of the physical education curriculum.

QUERIES AND MINOR NOTES

TREATMENT OF NEPHROSIS

TO THE EDITOR:—*In a 52-year-old woman, edema of the ankles and legs developed, without facial edema, nine weeks ago. She vomited twice in the morning. Urine examination showed albumin 4+, with 10 white blood cells, 3 to 4 red blood cells, and no casts. Blood pressure and optic fundi were normal. The red blood cell count was 4,800,000; hemoglobin was 95%; and the white blood cell count was 10,050, with 53% neutrophils and 40% lymphocytes. Blood chemistry showed normal blood urea nitrogen but a total protein of 4.7 gm. per 100 cc., with an albumin-globulin ratio of 1.6 to 1. Results of the Fishberg concentration test were normal. The temperature never exceeded 99.8 F. The heart and lungs were normal, as were an electrocardiogram and chest roentgenogram taken a year ago. During the following weeks, the patient was put on bed rest, and given a salt-poor and fat-poor diet, vitamin B capsules, liver extract, protein hydrolysate, and ammonium chloride. There was no change in the urinary findings, except for the appearance of hyaline casts. The daily total urinary albumin was between 6 and 11 gm. The total blood protein went down to 3.01 gm. per 100 cc., but the albumin-globulin remained above 1. The sedimentation rate was between 40 and 30 mm. per hour. Total cholesterol was 750 mg. per 100 cc., with the cholesterol esters about 65 to 69% of the total. Liver function tests were normal. Hematocrit was 46%.*

The edema could be checked moderately by the administration of ammonium chloride and occasional injections of 1 cc. of mercaptomerin (thiomerin) sodium; however, the effect was only temporary. A urine culture was done, but no growth was found. For a few days, gantrisin* (3-4-dimethyl-5-sulfanilamido-isoxazole) was given, with no effect, and, because the urine excretion diminished, it was discontinued. I had to stop the administration of liver extract and protein hydrolysates because the patient completely lost her appetite and felt nauseated. After discontinuation of these medications, the general condition improved. The urinary findings, together with the hypoproteinemia, the normal blood pressure, and the normal fundi warrant the diagnosis of chronic nephrosis. What other therapy is advised? What is the prognosis?*

Frederick D. Regensberg, M.D., Butler, Pa.

ANSWER.—Aside from the large number of red blood cells in the urinary sediment, the case described could be an example of pure lipoid nephrosis occurring late in life; the red cells suggest that this may be nephrosis occurring in the subacute stage of hemorrhagic glomerulonephritis. An antistreptolysin titer, done soon after onset, may be useful in confirming the latter diagnosis, as would careful studies of the sediment for red cell casts. In pure lipoid nephrosis, and, less often, in nephrotic stages of glomerulonephritis, the disease has been favorably altered by the use of nitrogen mustard, cortisone, or corticotropin. Spontaneous remission may occur after intercurrent viral infections. Diuresis, with no effect on the course of the disease, can be produced by administering 50 gm. of human albumin daily. High protein diets and hydrolyzed protein infusions have no favorable effects, but, as with albumin infusions, they actually increase proteinuria. Low fat diets and thyroid extract rarely alter the plasma lipid levels, which return to normal after proteinuria ceases. As the condition may last for months or years, bed rest is not advisable, but avoidance of fatigue and chilling is essential. Use of sulfonamides and antibiotics is futile, except for intercurrent infections. Dietary sodium restriction and mercurial diuretics, together with ammonium chloride and cationic exchange resins, are helpful in controlling edema.

The administration of 200 mg. of cortisone daily, in four oral doses, for 3 days and then 100 mg. a day for 10 days, with abrupt cessation of therapy, should be tried first. Remission may occur after the drug has been discontinued. Acetylsalicylic acid, in doses of 4 gm. daily, may markedly reduce proteinuria, but few remissions have resulted from the use of this agent. The life prognosis is usually good in older patients with nephrosis or those with subacute nephritis with normal blood urea. Recovery is rare in the latter, but it may occur spontaneously in about half of the former group.

LATE SEQUELAE OF DEEP ILIOFEMORAL THROMBOSIS

TO THE EDITOR:—*Twenty years ago a woman had a "milk leg" and pulmonary embolism following a delivery. Today both lower limbs are swollen, the left more than the right, and there are some superficial varices. She has been wearing elastic stockings for years, apparently without discomfort. I believe that she has deep thrombosis. It has also been my impression that patients with deep involvement cannot stand an elastic stocking; however, in this patient there can be no question of the deep involvement. The patient has been advised to have an operation. Is it not contrary to all reason and orthodox teaching that superficial varices should not be obliterated if there is a deep thrombosis? If the superficial femoral were ligated would the subcutaneous veins be able to carry on the circulation? My patient has unfortunately had some of the superficial veins obliterated by injection.*

M.D., Pennsylvania.

ANSWER.—The decision as to whether the late sequelae of deep, iliofemoral thrombosis are to be treated with well-fitting elastic hose from toes to groin, with ligation and stripping of the superficial varicosities, or with division of the deep venous system, cannot be made without a study of the nature of the venous insufficiency that remains after a thrombotic occlusion of the deep venous system. Many patients are comfortable with the elastic hose, show little swelling, and are only discomfited by attacks of phlebitis in the collateral veins, or by supramalleolar indurations, which may ulcerate on slight injury. In more than half of the patients who have suffered an iliofemoral venous thrombosis chronic recurrent ulcerations develop after 20 years. But, if the calves are soft, if the swelling is moderate, and if rapid muscle contractions of the calf by standing on the toes 10 to 15 times visibly empty distended superficial veins, a fair state of compensation exists, and no surgical therapy needs to be considered.

In other patients the superficial, communicating, and deep valves are incompetent, and a marked reflux of blood occurs from above when the patient is upright. Such a patient has an increased venous pressure in the lower extremities when standing. The usual Trendelenburg test gives an idea of how much of this reflux occurs through saphenous and communicating valves. The state of the deep valvular system can be studied by exercising the leg with a tourniquet placed just below the knee. If the superficial veins collapse on exercise and stay collapsed, the deep veins are patent and competent; if the veins collapse and refill after the exercise, the deep venous system is incompetent; if the veins do not collapse on exercise but distend even more, the deep venous system is obstructed. Only after demonstration of the deep valvular incompetence can one consider a ligation of the deep veins, but this clinical test should be corroborated with a suitable venogram. Not more than 10% of all patients suffering from post-thrombotic sequelae will satisfy these criteria; nor will postphlebitic lymphedema improve. The level of deep venous interruption is more effective at a popliteal, than at a superficial, femoral level. (See de Takats, G., and Graupner, G. W.: Division of the Popliteal Vein in Deep Venous Insufficiency of the Lower Extremities, *Surgery* **29**:342 [March] 1951.)

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

CONGENITAL DEFECTS

To the Editor:—*A woman was delivered at term in 1947, at the age of 25, of a normal female child. The second child, a male, was delivered in 1949. At three weeks the infant presented hoarseness, weakness and intermittent cyanosis with no physical findings. Chest x-ray showed a massively enlarged thymus. He received three x-ray treatments at weekly intervals and seemed to improve. He died suddenly two days after the third treatment. Autopsy revealed the enlarged thymus, atelectasis of the upper lung lobes, and a patent foramen ovale. The third pregnancy began as a threatened abortion in November, 1950, but was carried with progesterone and limitation of activity. Several days past the expected date of confinement, delivery was medically induced, since life had not been felt for 24 hours. The patient was delivered of a stillborn male, externally normal. The mother is Rh positive. Autopsy was refused, and the only explanation I could give was the possibility of another organic congenital anomaly. The parents now want to know the probabilities of future congenital anomalies and whether pregnancy should be risked again.*

Fred H. McClain Jr., M.D., Mount Union, Pa.

Answer.—There is no apparent special reason to fear an abnormal fetus in this patient. Her first baby was normal. Her second baby had no gross defect. The thymus is considered by many to be enlarged normally at birth and requires no treatment. The foramen ovale is often open anatomically but not functionally. The cause of death probably was the atelectasis. The third baby could have died from almost any cause, since autopsy was not done, but there is no reason to suspect a congenital defect. A mother with one congenitally defective baby is no more likely to have a repetition than is the average patient. A mother with two defective babies is more likely to have a repetition. A woman with three defective babies is likely to have defective babies rather consistently.

DERMATITIS FROM DIESEL OIL

To the Editor:—*A railway opened a diesel shop in Chattanooga, and, since its beginning, three years ago, I have had several patients with allergic dermatitis, which appears to be due to contact with diesel oil. I wonder if this condition is commonly noted in similar shops. If so, is there any successful treatment, or possible prevention, by the use of a film to cover the skin?*

Cecil E. Newell, M.D., Chattanooga, Tenn.

Answer.—Dermatitis from diesel oil is oftener of the contact variety than of the allergic type. Sensitization is possible, but it is unlikely that it would be due to the oil per se; it is probably due to the aberrant proteins of the skin resulting from the contact damage. Also, after contact injury the skin may respond more readily to the allergenic qualities of soaps and other offenders. Diesel oil is a crude petroleum fraction similar to fuel oil, and, thus, is not outstanding as an allergen. The common severe injuries from diesel oil and diesel motors are from flesh penetration from high pressure jet streams received when the oil is thrust into the combustion chambers. This deeply imbedded oil provides traumatic injury and not essentially a dermatitis. The practice of cleaning the skin with this oil is indefensible and should be condemned. Some protection is afforded by hand coatings. Ordinary protective ointments and lotions are of dubious value.

VITAMIN A AND DEAFNESS

To the Editor:—*In the September issue of* Coronet *magazine is an article entitled "Five New Cures for Deafness," by Madelyn Wood. One of these cures mentions the use of large doses of vitamin A. I would like to have an authoritative opinion regarding the use of such doses of vitamin A.*

M.D., Tennessee.

Answer.—There exists very little scientific evidence for the claim that large doses of vitamin A are beneficial in cases of deafness. Until there have been further published reports of carefully controlled series of cases, this treatment must be regarded as experimental and not of accepted value.

EXPOSURE TO AZOBENZENE VAPOR AND TOBACCO SMOKE

To the Editor:—*A 58-year-old man has worked in a greenhouse for about 10 years, using a compound containing azobenzene and nicotine for fumigation purposes. This is applied by heating the substance, which causes an orange-colored vapor to appear throughout the greenhouse, which is allowed to remain for a period of hours, at the end of which the employee puts on a gas mask and opens all the windows. Except for acute conjunctivitis from contact of the eye with insecticide, he had been in reasonably good health until six weeks ago, when he became acutely ill, with extreme weakness, chills, and a temperature of 104 to 105 F. He was treated with penicillin on the second day of his illness, which was undiagnosed; after this severe soreness and inflammation of the throat, with considerable blindness, developed. This later condition is considered to be acute superficial punctate keratitis of both eyes. Now, six weeks after the original onset, the throat has almost cleared and the eye condition is improving slowly. The patient has had no contact with the azobenzene and nicotine compounds since the beginning of the illness. I would like information on poisoning by azobenzene and nicotine.*

M.D., Illinois.

Answer.—The fumigator used by the patient appears to be similar to a pressure fumigator described by Blauvelt (New Azobenzene Fumigants, New York State Flower Growers Bull. No. 19, 1947, p. 9.) This device releases clouds of azobenzene vapor and tobacco smoke from a special container holding a mixture of powdered tobacco, potassium nitrate, and azobenzene and which is ignited by means of a "sparkler." The toxic properties of azobenzene are poorly understood, and there is little published clinical data on this compound. By contrast, the injurious effects of nicotine are well known. The acute conjuctivitis may have been caused by exposure to the tobacco smoke, since nicotine and other constituents of the smoke are fairly strong irritants. In addition to conjunctivitis, nicotine may also cause scotoma, narrowing of the field of vision, and diminution of the sharpness of sight in the center of the visual field. The subsequent signs of muscular weakness, chills, elevated temperatures, and inflamed throat could also be caused by exposure to tobacco powder or smoke (Stevenson, H. M.: Acute Nicotine Poisoning as Noted in Manufacture and Use of Nicotine Insecticides, *California & West. Med.* **38:**92, 1933). Although subnormal temperature is commoner in nicotine poisoning, temperatures up to 104 F have been reported (Deacon, J. N.: Poisoning by Tobacco applied to the Skin, *Brit. M. J.* **2:**61, 1926; Price, J. P.: Acute Nicotine Poisoning with Fatal Outcome in a Child, *Am. J. Dis. Child.* **57:**102, 1939). The prognosis in nonfatal cases is usually favorable.

HYDROGEN SULFIDE GAS IN INDUSTRIAL PLANT

To the Editor:—*The workers in an industrial plant have been annoyed by the odor of hydrogen sulfide gas emanating from die cutting machines. The source of this gas apparently is a cooling solution made from vegetable oils and water. Since the gas is most noticeable during the summer months and after the machines have been standing idle over the week-end, it is suspected that bacterial action might be the cause. Your advice will be appreciated.*

John D. Lynch, M.D., Manitowoc, Wis.

Answer.—The situation described is of common occurrence in the metal fabricating industries. Experience indicates that in the usual situation the quantity of hydrogen sulfide gas is not sufficient to create systemic hydrogen sulfide poisoning, even though that gas is toxic. As mentioned, the offensive odors provide the major disturbance. Many cutting compounds contain added sulfur derivatives, and some oils contain sulfur compounds. In either situation, decomposition leading to the liberation of hydrogen sulfide is readily accomplished, and perhaps is brought about through bacterial action, but some chemical disintegration may arise apart from gross bacterial participation. The remedy for this may be found in the more frequent changing of the supply of the cutting oils without prospective reuse. At the time of oil changing, all possible cleansing of tanks, pipes,

and other parts should be done. During hot weather the lifetime of some cutting agents does not exceed one week. Available to manufacturers are several disinfectants, including quaternary ammonium compounds, capable of hampering bacterial growth and action. Such compounds do not sterilize oils, but they do reduce the quantity of bacterial growth to a negligible level. Some manufacturers have reached the conclusion that it is better to discard offending compounds at frequent intervals than to resort to chemical disinfection.

LIGATION OF FEMORAL VEIN

To the Editor:—*What are the indications for ligation of the femoral vein? May the femoral vein be ligated in a patient whose long saphenous vein previously has been ligated and injected?*

J. F. Brennan, M.D., Clarksburg, W. Va.

Answer.—Ligation of the superficial femoral vein is indicated as a preventive measure in amputations of the lower extremities or any other operation below the level of the groin that results in prolonged immobilization or impaired muscle action. In the presence of an acute, deep venous thrombosis at the calf or at popliteal level, it is advised by some who do not use anticoagulants. It is certainly advised when anticoagulants cannot be used, as in the presence of bleeding surfaces, or in hemorrhagic blood dyscrasias. In chronic deep venous insufficiency, when the canalized thrombus destroys the valves, its use is highly debatable. Should reflux of the deep veins be demonstrable by tests and by visualization of the deep venous system, the popliteal level is preferable to the femoral level. Common femoral vein ligation results in persistent edema. Previous obliteration of the long saphenous vein does not contraindicate per se a ligation of the superficial femoral vein, but, if the profunda is left unligated, the reflux will establish itself through the patent and incompetent popliteal vein. The technique of these exposures follows the classical methods for ligating the arteries, to which they often adhere.

TREATMENT OF PARKINSONISM

To the Editor:—*Please discuss the latest treatment for Parkinson's disease.*

William Bayne Allen, M.D., Kansas City, Mo.

Answer.—Therapy in Parkinsonism continues to be symptomatic. Relief of symptoms, when obtained, is only partial. New synthetic antispasmodics have proved more effective than the older belladonna preparations. In this country, trihexyphenidyl (artane®) has been the most popular of the antispasmodics. It is the opinion of most authorities that trihexyphenidyl, in doses of 2.5 to 5 mg. three times a day is, at the present time, the most efficacious medication. The addition of diphenhydramine hydrochloride (benadryl®), in doses of 50 mg. three times a day, to the above medication may potentiate the action of the trihexyphenidyl. Toxic symptoms are manifested by unsteadiness, dryness of the mouth, visual blurring, and, occasionally, by mental confusion. For certain patients, the belladonna derivatives continue to be the drugs of choice.

It is not sufficient to give patients with Parkinsonism medicine. Usually, they also demand and need considerable emotional support and some readjustment of their life situation. Proper physical therapy, with heat, massage, and exercise, often proves beneficial.

EXTRASYSTOLES

To the Editor:—*I note in several standard works of medicine that extrasystoles assume clinical importance when they appear or increase in frequency during the period of deceleration after exertion. This seems contrary to my experience.*

Henry G. Hadley, M.D., Washington, D. C.

Answer.—The statement cited is not borne out by the experience of most observers. In general, extrasystoles are more apt to occur when the heart rate is slowed, particularly during the period of slowing that follows exertion or that occurs during rest. They are generally eliminated temporarily by any factor that increases the heart rate, such as exertion and nitrites. For this reason, it is the consensus that extrasystoles attain greater clinical significance if they occur during tachycardia or when the heart is accelerated by exercise. However, this is not a universal rule, since extrasystoles of functional origin may also be precipitated by exercise. Therefore, the heart rate at which extrasystoles appear is not an infallible criterion to determine clinical significance of extrasystoles.

MAINTENANCE THERAPY AFTER RAPID DIGITALIZATION

To the Editor:—*I would appreciate an opinion on the follow-up dosage of digitalis leaf, or digitoxin, following the initial use of lanatoside C ("cedilanid") intravenously. There appears to be a difference in procedure with regard to dosage in different institutions. Assuming 8 cc. of lanatoside C given intravenously has proved to be the effective dose, will the immediate continuation of maintenance doses of digitalis leaf or digitoxin maintain adequate digitalis effect? Or, because of the more rapid elimination of lanatoside C from the system, would it be expected that additional doses of digitalis leaf or digitoxin would be necessary before starting the maintenance dosage? The patient weighs between 125 and 175 lb. (56.6-79.3 kg.) and is not elderly. The patient has received no previous digitalis.*

M.D., California.

Answer.—Initial consideration of a few points about digitalis therapy is of prime importance. 1. Many different techniques of digitalis therapy are authoritatively advised and seem to be satisfactory. There is probably no one best method. 2. It is rarely necessary to digitalize any patient rapidly, and, therefore, the problem stated is not as important in current practice as it once was. Disagreeable toxic effects from digitalis are so common that it is important to avoid emergency treatment with large doses of digitalis, except when absolutely essential. 3. Strophanthin and ouabain are still satisfactorily used in emergencies in other countries, and in such countries booster doses of digitalis are not routinely used afterward.

It is sufficient in most cases to begin a simple maintenance dose of digitalis leaf, digitoxin, or digoxin orally immediately after the emergency treatment; however, some authorities recommend slightly larger doses of the maintenance drug for a few days before routine chronic treatment. Each case should be considered individually as to whether there is any need for the booster doses.

MATTRESS FOR PERSONS WITH NORMAL BACKS

To the Editor:—*What is the best type of mattress for persons with normal backs? Do you recommend innerspring mattresses? Do you recommend the new foam filling?*

Angela Quilici, M.D., San Carlos, Calif.

Answer.—In considering bedding equipment for the normal person, attention must be directed toward both the mattress and the springs. If the springs sag, the mattress placed on it will sag. For proper sleeping posture, the first essential is a good foundation, springs that will not sag. Box springs and other types, if well made, provide this foundation. The mattress used should give firm support, yet have sufficient surface softness to be comfortable. Certain innerspring mattresses have been designed to provide this firm support and surface softness. The foam rubber mattress, with specially constructed springs, and the innerspring mattress, with its set of springs, seem to provide proper bedding equipment for the normal person.

MENSTRUAL MIGRAINE

To the Editor:—*In the treatment of menstrual migraine, I have had good results from the use of testosterone given 10 days before each expected period. Would a dose of 50 mg. of testosterone each month have harmful effects?*

M.D., Tennessee.

Answer.—The chances that 50 mg. of testosterone propionate administered once monthly would cause virilism or other harmful changes are slight. There is the possibility, however, that this dosage may delay the onset of the menses.

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